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ARTERIAL INSUFFICIENCY AND GANGRENE OF THE LOWER EXTREMITY

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The complexities of gangrene and of arterial insufficiency of the lower extremity may be simplified by a study of the gross vascular pathologic anatomy by clinical arteriography. When utilized with other basic approaches it may lead to the saving of a limb. This problem is of great importance in as much as arterial insufficiency and gangrene of the foot are the most common diseases on the surgical ward, and as longevity increases, this disease will become even more frequent.

Clinically, no symptoms or other evidence of arteriosclerosis may exist in spite of the extensive distribution of atherosclerosis often found at necropsy. Most organs are "hidden" within the body and their functional reserve further suppresses clinical manifestations. In contrast, the lower extremity is visible and directly accessible. Arteriosclerosis may often be diagnosed in its early asymptomatic stages simply by physical examination of the lower extremity, supplemented by funduscopic examination of the eye and by a study of other surface manifestations.

The most common cause of arterial insufficiency in the lower extremity is, by far, arteriosclerosis. Although, in the description of a disease, symptoms are usually presented first, followed by the signs, in sclerotic arterial insufficiency of the lower extremity, the actual presence of signs precedes the onset of symptoms, and are visible and accessible for examination. Quite frequently, the signs of sclerotic arterial insufficiency without any referable symptoms are observed in patients with totally unrelated diseases. In the clinical appraisal, the *diagnosis* of arterial insufficiency must be made first, and then its *etiology* considered. The diagnosis of arterial insufficiency can be made either from the objective findings alone or by both the signs *and* symptoms. The first problem therefore, is to determine the presence of signs of arterial insufficiency.

SIGNS OF ARTERIAL INSUFFICIENCY

The *signs* of arterial insufficiency of the lower extremity may be elicited by *inspection* and by *palpation*. Arterial insufficiency results in ischemia. Ischemia of the hair follicles results in absence of hair on the leg; ischemia of the sweat glands and of the sebaceous glands results in dryness of the skin; ischemia of the nails results in grotesque shaped nails (termed onychogryposis); and ischemia of the squamous epithelium results in thin, parchment-like, shiny skin —all visible on inspection. With intense degree of arterial insufficiency, *color changes* of the foot, and sometimes of the leg, are noted. At first, these color changes can be elicited only by positional change of the extremity. Upon elevation, the foot assumes a cadaveric pallor. In a dependent position, it develops a cyanotic rubor. The longer the time required for the onset of the redness after lowering the foot, the greater is the

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degree of insufficiency and also the more intense will be the eventual cyanotic redness. With extreme degrees of insufficiency, the cyanotic redness is noted even with the leg and foot in the horizontal position. The persistence of intense cyanotic rubor is often indicative of an impending gangrenous state.

That an arterially insufficient foot should appear red may seem paradoxical. Normally, the arteries, pulsating against the contiguous veins, act as venopressor agents and, aided by the venous valves, maintain a unidirectional flow of blood in the veins. The cyanotic hue may be evidence of the stasis of venous (deoxygenated) blood due to the absence of this particular venopulsion mechanism.

Upon palpation, three types of data are obtained:—(1) temperature changes, (2) the pulsations, and (3) the physical state of the skin.

Physical examination for *temperature* consists in determining, first, whether the leg and foot are cool or warm, and second, whether a critical temperature level is present. Normally, a gradually decreasing temperature is detected as the examiner's hand descends distally over the skin surface of the extremity. However, when a major vessel occlusion is present, a sudden drop in temperature is detected at a level distal to the arterial occlusion. For example, in a popliteal occlusion by an embolus, the leg suddenly becomes cool just above the ankle. This level is known as the critical temperature level. The oblique course of the branches from the central major vessels to the periphery in the extremity results in preservation of the normal warmth of the skin for a distance beyond the actual level of occlusion.

The unilateral absence of the femoral pulse at the groin indicates an arteriosclerotic occlusion of the common or external iliac artery; bilateral absence indicates an arteriosclerotic occlusion of the lower aorta or, rarely, coarctation. In the absence of a pulse at the groin no pulsations will be found distally, for, once the arterial pulsation in the lower extremity is lost because of a major vessel occlusion, it is not regained through collaterals. However, as is usually the case, the pulsations of the femoral artery in the groin are found, and the popliteal artery is next sought, deep within the the popliteal fossa. This pulsation is often difficult to detect. Distally, the dorsalis pedis artery, the continuation of the anterior tibial artery, is located, usually between the first and second metatarsal bones of the foot and immediately lateral to the extensor hallucis longus tendon. The posterior tibial artery is located immediately inferior and somewhat posterior to the medial malleolus. Caution must be exercised to prevent misinterpretation of the pulsation in the examiner's finger tips as pulsations in the patient's foot. The presence of arterial pulsation of these distal vessels in the foot implies a continuous patency of the major vessels above, from the aorta through the iliacs, femoral, popliteal and tibial vessels, and hence indicates good major vessel supply. The presence of these distal pulsations in the foot practically rules out arteriosclerotic arterial insufficiency.

Ateriosclerosis usually refers to intimal disease (atherosclerosis) which leads to occlusion of a lumen. It occurs in the larger vessels, particularly the aorta, iliac, femoral and popliteal arteries. Since it is normally difficult to palpate the popliteal pulse, determination of the level of an occluded main artery in the presence of a femoral pulse and the absence of a posterior tibial and dorsalis pedis pulse is possible only by oscillometry and can be confirmed by arteriography.

Upon palpation, lastly, the thinness and dryness of the skin may also be noted.

Other examinations in the evaluation of the circulatory status include: (1) an ordinary x-ray of the extremity for calcific deposits in the vessels and for confirmation of muscle atrophy; (2) surface temperature determinations by instrument, and (3) arteriography.

SYMPTOMS OF ARTERIAL INSUFFICIENCY

The *symptoms* of arterial insufficiency of the lower extremity may be classified in an anatomical pattern thusly:

(1) *Ischemia of muscles.*
   a. excessive tiredness of legs—in the early stages.
   b. intermittent claudication—its site

depending on the location of the occlusion. The pain is characteristically brought on by the effort of walking, and is relieved by rest. After a period of rest, the individual again may walk a similar distance. This sequence of events —effort leading to pain, rest giving relief of pain and permitting further effort—is highly diagnostic, and differentiates the pain of arterial insufficiency from other causes of pain, such as "sciatica."

c. Pain occurring during rest, such as that which may awaken patients from their sleep, indicates a severe degree of insufficiency—if the insufficiency is not caused by the inflammatory vessel and nerve changes of Buerger's disease. This "rest" pain indicates the important influence of muscle contraction on the circulation. A contracting muscle not only shortens the distance between its origin and insertion, but enlarges in its diameter, thereby pushing against and compressing adjacent vessels. This factor is seemingly important enough to bring on pain in those with a reduced blood supply.

(2) *Ischemia of the nerves* produces various paresthesias, such as numbness, tingling, and burning.

(3) The patient may complain of the actual coldness of the skin of the extremity.

OSCILLOMETRY

When the dorsalis pedis or posterior tibial pulse is not definitely present in the foot, oscillometry is indicated, inasmuch as the absence of the distal pulsation in the foot indicates a major vessel occlusion at some superior level. Because the popliteal pulse is difficult to detect, the level of occlusion somewhere between the femoral pulse at the groin and the non-pulsating dorsalis pedis vessel in the foot is difficult to detect by ordinary peripheral examination but is detectable by oscillometry. The Collens sphygmo-oscillometer, though not a sensitive oscillometer, is a reliable indicator of a major vessel occlusion, accurately localizing the level of occlusion. No oscillations whatever are detected distal to an occlusion of a major vessel, such as the femoral or the popliteal, or of all three major leg vessels. Diminution in the range of oscillometric fluctuation is generally indicative of narrowing. But the important concept is that oscillometric fluctuation *per se* is indictive of continuous patency to the level being examined. A pulsating type of blood flow exists providing the vessels are continuously patent, regardless of how narrowed the lumen may be and regardless of how slight the fluctuation. This point was vividly demonstrated in the case of a traumatic severance of the femoral artery by a bullet which, after suturing, left an extremely small-sized lumen at the line of anastomosis, as was demonstrated by arteriogram. Yet, a dorsalis pedis pulsation was detectable. The Collens sphygmo-oscillometer is, thus, useful in determining continuous patency, occlusion, or narrowing of the major vessels. The instrument does not appear sufficiently sensitive to measure collateral circulation, and thus is more valuable because the fluctuation of the major vessel's pulse is not confused on the instrument by collateral flow.

ARTERIOGRAPHY

A vivid, anatomical evaluation of the functional insufficiency may be obtained by outlining patent, narrowed or occluded vessels by arteriography. Arteriography is indicated if the oscillometer fails to oscillate at a particular level, indicating occlusion of a major vessel. When the oscillometer fluctuates distally in the leg, no additional information can be obtained by the arteriogram, as it will show the major vessels to be continuously patent and will merely confirm an interpretation that can be made from oscillometry alone. However, the absence of oscillations below the knee in the presence of a femoral pulse at the groin indicates a block of the femoral or popliteal artery. The oscillometer permits localization of the superior or proximal limit of the occlusion at a specific level in the thigh. The arteriogram furnishes this information too, but, in addition, indicates the exact length of the occluded segment, *i.e.*, how far distally the major

vessel remains occluded. Furthermore, the arteriogram reveals the status of the portions of the artery which have remained patent both proximal and distal to the occluded segment. It also reveals major collaterals and the extent of smaller collaterals which have become discernible. Occlusions most frequently occur in the popliteal artery and next most frequently in the femoral. Infrequently, both the femoral and popliteal are occluded, leaving collaterals to carry blood distally. The profunda artery is rarely occluded and, in the presence of superficial femoral and/or popliteal occlusion, becomes the major source of blood supply distal to the occlusion.

CLINICAL VALUES OF ARTERIOGRAPHY

Besides the enlightening and basic data, arteriography of this region is of clinical value. Its simplest value applies to the determination of levels of amputation for a gangrenous foot. Usually, in arteriosclerotic gangrene a supracondylar level (above the knee) of amputation is required for uncomplicated healing of the stump. Actually, however, if the main blood vessels are open and in continuity as far distally as below the knee or to the ankle region, a below-the-knee amputation may reasonably be expected to heal. A below-the-knee stump permits the patient much greater maneuverability. This becomes of great importance in those patients who eventually become bilateral amputees. Bilateral amputees are particularly helpless if the amputations are bilaterally supracondylar. A patient who had a supracondylar amputation on one side and a below-the-knee amputation on the other side gratefully attested to the far greater usefulness of the below-the-knee stump. The determination of the possibility of a below-the-knee amputation when the major vessel patency continues uninterrupted to the vicinity of the knee is impossible by the oscillometer. The bony prominences of the knee prevent adequate transmission of arterial fluctuation to the oscillometer. In the presence of a popliteal occlusion just above its bifurcation, the oscillometer will fail to fluctuate from as high as just above the knee — the knee region being silent. Hence, with the oscillometer, one cannot determine the actual level of occlusion from levels just above the knee down to the upper calf. Hence the arteriogram is valuable when oscillometric fluctuations are present above the knee and absent below the knee.

Secondly, the arteriogram is of great clinical importance as an indicator and guide to vascular surgery of the extremity for arterial occlusion. This has become true only since vascular surgery has become practical. The exact site of occlusion and the length of occlusion is roentgenologically visualized, thus permitting accurate surgical approach. The occluding segment may simply be removed *per se* for the presumed purpose of removing a source of antidromic vasoconstrictor impulses which cause vasoconstriction distally. The occluded segment of the artery may be removed and replaced by a vessel graft—either a vein or an artery segment, which may be either autogenous or homologous. An endartectomy of the occluded segment may be done. Endartectomy consists of removing or reaming out the inner occluding layers of the occluded segment of the artery to re-establish continuity or patency of the lumen. Occasionally, an arteriovenous fistula is surgically produced for the purpose of either arterializing a vein or of increasing the blood supply by the usual physiologic mechanisms of an arteriovenous fistula. This also requires roentgenologic arterial visualization to determine the availability of a patent artery for such a procedure.

ETIOLOGY OF ARTERIAL INSUFFICIENCY

The diagnosis of arterial insufficiency having been made, the etiology of the insufficiency must next be determined. The three most commonly considered diseases are (1) arteriosclerosis, (2) thrombo-angiitis obliterans or Buerger's disease, and (3) Raynaud's phenomenon. By far the most common cause of arterial insufficiency is arteriosclerosis. Other less common causes are aneurysms of peripheral arteries and arteriovenous fistulas. In a given case, the various characteristics of a disease may be diagnostic, and lend further enlightenment to the na-

ture of the disease.

The age and sex may aid in the diagnosis—the male suffering from either arteriosclerosis or Buerger's disease and the female from either arteriosclerosis or Raynaud's disease. The age serves to further differentiate. Involvement of the upper extremity usually indicates Buerger's or rarely arteriosclerosis in the male, and Raynaud's in the young female. Pain is mild to moderate in arteriosclerosis and severe in Buerger's or Raynaud's.

In the presence of gangrene, an additional clinical entity, diabetic gangrene, must be differentiated from the above considered diseases. Major vessel occlusion does not play a pathogenic role in diabetic gangrene. Thus, an intact major arterial circulation also helps in the diagnosis of the type of gangrene. The patient with arteriosclerotic gangrene frequently maintains a sitting position so that the feet may hang down in a dependent position. Gravity apparently improves the blood flow to the foot, and this position usually ameliorates the pain of ischemia. The patient with diabetic gangrene, having a comparatively much better blood supply, keeps the leg and foot horizontal in bed. The patient with Buerger's disease, because of the excruciating pain on movement, holds his feet in the palm of his hands gently and carefully, to protect them from any motion.

The gangrene in Buerger's disease is often patchy, involving only portions of one or more digits, and requiring, in early stages of the disease, only minor amputation, such as a portion of a toe, in contrast to the usual supracondylar level required for arteriosclerotic gangrene. In Raynaud's disease, gangrene does not usually occur, but may do so after many years of recurring episodes· especially after arteriosclerosis has supervened. This correlates well with the size of the vessel primarily involved. The gangrene of arteriosclerosis is secondary to an occlusion of a large major vessel, the gangrene of Buerger's disease is secondary to segmental occlusions of the medium-sized vessels, and gangrene in Raynaud's disease *per se* is the result of involvement of arterioles. Thus, decreasing degrees or severity of gangrene occur parallel to the decreasing size of the involved vessel.

SYMPATHETIC ROLE IN ARTERIAL INSUFFICIENCY

A modern approach towards possible improvement of the blood supply consists in possible changes of the vasomotor tone through the sympathetic nervous system. This system, centrally, consists of two ganglionated chains, one placed along each side of the vertebral column and extending from the upper cervical to the lower sacral regions. The thoraco-lumbar portion of the chain receives communicating fibers from the spinal cord, specifically from the antero-lateral column through the anterior horn and anterior nerve root. This is known as the thoraco-lumbar outflow, the connecting fibers to the chain being known as the white rami communicantes. The grey rami communicantes carry the efferent fibers from the ganglionated chain to the somatic nerves, arising from the chain as high as the cervical chain and as low as the sacral portion of the chain. The fibers from the cord reaching the chain may synapse at the same level as they enter the ganglion of the chain, or the fibers coming in from the cord may course upwards or downwards in the chain for a variable distance before reaching synaptic junctions at higher or lower levels. From the synapse, a ganglion cell leads to a somatic nerve at that level. Also, from the thoracic part of the sympathetic chain, the greater, the lesser and the least splanchnic nerves arise as fibers coursing from the spinal cord (antero-lateral column) through the anterior nerve root, and through the ganglionated chain, without stopping to synapse in the chain. These splanchic nerves supply or gather with ganglionic plexuses before reaching the abdominal viscera. The fibers immediately proximal to the viscera course along those vessels supplying the respective viscera. An important anatomic distinction between sympathetic nerve supply to the viscera and to the soma *per se* is that the viscera receives its sympathetic innervation by way of the blood vessels which carry the fibers within their adventitia, whereas the so-

matic sympathetic innervation to the extremities, for example, is carried by the spinal nerves which give off sympathetic fibers at intervals to the vessels coursing alongside the somatic nerves.

Somatically, the sympathetic impulse stimulates (1) the sweat glands, (2) the errectori pilorum muscles, and (3) the tonus of the arteries. The vessels more directly affected, however, are those near the skin surface and those in the subcutaneous tissues, whereas those vessels supplying the muscles *per se* are not affected directly by the sympathetics.

Basically, a given arterial vessel maintains its average size by a certain degree of sympathetic stimulation to its muscle; vasoconstriction resulting from an increased sympathetic impulse. Inhibition of the sympathetic impulse results in dilatation, not only from the constricted state, but to the total or completely atonic, dilated state of the normal vessel. The organic arterial occlusion resulting in insufficiency is, at present, ordinarily beyond remedy *per se*. Interruption of the sympathetic impulse offers the possibility of vascular improvement through the possible resulting arterial dilatation. Actually, however, this avenue of improvement is usually insufficient to be clinically significant. But, to determine which particular patient with arterial insufficiency may be benefited by sympathectomy, an individual case study is necessary.

PREOPERATIVE PROGNOSIS OF SYMPATHECTOMY

Surface temperature determinations of the lower extremity reveal normally a gradually decreasing temperature, as can be noted upon palpation. Thermometry indicates a range from about 34°C in the thigh to approximately 31°C over the calf, 29°C over the dorsum of the foot, and to about 25°C over the great toe. The extent of the decrease varies somewhat with the environmental temperature and the humidity. This study is made after the lower extremity is exposed to the air for at least one-half hour so that the surface temperature of the skin may become stabilized in equilibrium with the environmental temperature. The toe varies normally from about 30°C to the lower 20's°C. The distal decrease in the temperature of the surface represents the *vasoconstrictor gradient*. This is readily appreciated when a uniform temperature of about 34°C from thigh to tip of toe is noted following lumbar sympathetic block. The greatest degree of vasoconstriction thus occurs in the toes, and thus changes are most readily noted in the toes. Incidentally, the surface temperature measures the *rate* of blood flow through the skin.

Thus, to evaluate the possibility of improvement of the ischemia of an extremity through sympathectomy, the surface temperature response of the extremity to a procaine lumbar sympathetic block of the same side is determined. In a vascularly normal extremity, the temperature should rise to a uniform degree, approximately 34°C throughout, from thigh to toe. However, a rise of 1°C or more, following a lumbar sympathetic block, does indicate possible improvement of the blood supply by sympathectomy. Also, the *difference* between the temperature attained following a sympathetic block and the full 34°C is the *occlusion index*, indicating that organic occlusion is present, to that extent, diminishing the blood flow to the skin.

The value of sympathectomy further varies with the disease process. In Raynaud's disease ablation of the sympathetic impulses to the extremity involved is usually highly beneficial inasmuch as this disease is essentially vasospasm. In thrombo-angiitis obliterans and other inflammatory lesions involving the vessel wall, such as trauma or thrombophlebitis, the vasospasm associated with the inflammation is intense. Hence, sympathectomy is of value in Buerger's disease for alleviating this vasospasm. Of course, sympathectomy has no influence on the organic occluding process of this disease. Sympathectomy is indicated particularly, however, early in this disease when the vasospasm plays the major role. But only if abstinence from tobacco is strictly adhered to, will the sympathectomy yield even a fair result.

In arteriosclerosis obliterans, the process is apparently not inflammatory, and appears to elicit very little vasospasm.

Furthermore, the obliterating process usually occurs slowly so that collaterals have ample time to functionally develop *pari passu* with the narrowing. Thus, an evaluation of the arterial flow in an extremity with arteriosclerosis obliterans, at a given time, usually includes the total collateral flow as well as the major vessel flow. Hence sympathectomy is of limited value in arteriosclerotic insufficiency. However, a transitory warming of the skin is noted quite often following sympathectomy. The sympathetic nerves supply the vessels of the skin and subjacent tissues, and not the muscles from which intermittent claudication actually stems. Hence, it may seemingly improve only the most superficial tissues. In the development of gangrene, however, it is the outermost layer, the skin, which is the protecting layer against the environment and infection. When viability of the skin layer is impaired, life is jeopardized. In the stage of early impending arteriosclerotic gangrene, the gangrenous process may be stayed for a short time by transitorily increasing the blood supply to the skin by sympathectomy. The development of gangrene is not prevented ultimately by this procedure, as the mechanism of occlusion (thrombosis of the digital artery through stasis) is not essentially affected by sympathectomy.

Procaine blocks of the lumbar sympathetic chain may also be done for its transitory therapeutic value. Daily, repeated blocks, each followed by a palpable warming of the extremity, not only maintain the improvement for several hours, but frequently, after 4 or 5 such blocks, appear to enable the warmth to persist for several days without additional blocks. This is also valuable treatment during the pre-operative work-up of the patient. Lumbar sympathetic blocks are of distinct therapeutic value in those instances of transitory vasospasm of the lower extremity following trauma, in association with thrombophlebitis, and frost bite.

Even though the status of the vessels is such that no rise in surface temperature occurs with a sympathetic block, it may be difficult to ascertain whether the sympathetic chain was actually blocked. Dryness of the skin (effect on sweat glands) cannot always be used as a criterion because of the ischemic atrophy of the sweat glands. Occasionally, a delayed response may be noted, such as increased warmth of the leg occurring on the day following the block. Because of the difficulty in interpreting negative responses, patients frequently are subjected to sympathectomy for possible benefit in spite of a negative procaine block.

PRINCIPLES OF SYMPATHECTOMY

Sympathectomies may be classified into preganglionic and postganglionic types. They may consist of removal of the lumbar chain for sympathetic denervation of the somatic nerves forming the sacral plexus, or of removal of the upper thoracic chain for sympathetic denervation of the somatic nerves forming the cervical and brachial plexuses. It has been stated that post-ganglionic sympathectomy sensitizes the end-organs to circulating adrenalin, and hence may aggravate instead of relieve the vasospasm. Hence, pre-ganglionic sympathectomy is preferred. The lumbar sympathetic chain is usually approached surgically through a somewhat elongated McBurney type of incision, in which, however, the rectus sheath and muscle are incised, if necessary, for adequate exposure. This depends on the body habitus and the distance between the costal margin and the iliac crest. The vertebral column is approached retroperitoneally, with the dissection of the abdominal wall down through the transversalis fascia to the peritoneum. The intact parietal peritoneum is gradually retracted medially in a plane which leaves the ureter anteriorly adherent to the peritoneum with the genito-femoral nerve remaining posteriorly on the anterior surface of the psoas major muscle. The sympathetic chain lies on the anterio-lateral surface of the lumbar vertebral bodies, usually anterior to the lumbar vessels, except the fourth. It is situated more or less between the vertebral column and the psoas muscle, and can be accurately located in this area by palpation. On the right, the vena cava overlies it, and on

TABLE I

Symptoms and Signs of Arterial Insufficiency of the Lower Extremity

SYMPTOMS:	Ischemia of Muscles:	(a. Excessive tiredness of legs (b. Intermittent claudication (c. Rest pain
	Ischemia of Nerves:	(Paresthesias—such as numbness, tingling and burning
	Ischemia of Skin:	Coldness
SIGNS:	(Ischemia of Hair Follicles:	Absence of hair on leg
INSPECTION (a)	(Ischemia of Sweat Glands and Sebaceous Glands:	Dryness
	(Ischemia of Squamous Epithelium:	Thin, parchment-like skin
(b)	Color Changes:	(a. On elevation—cadaveric pallor of foot (b. On dependency—cyanotic rubor (c. Cyanotic rubor in horizontal position indicates an intense insufficiency and impending gangrene
PALPATION:	General temperature change, critical temperature level Pulsations—femoral, popliteal, posterior tibial, and dorsalis pedis	

the left, the aorta is just medial to the chain. There is considerable variation in the number of ganglia of the lumbar chain.

Infrequently, sympathectomy appears to hasten the process of impending gangrene or of marked arterial insufficiency to the point of actual gangrene. This paradoxical untoward result appears to occur when other regions, such as the pelvis, are also denervated by the same sympathectomy, causing vasodilatation of the vessels supplying the pelvis, and leaving less blood available for the vessels supplying the leg and foot. This paradoxical result may sometimes be predicted prior to sympathectomy when procaine block of the lumbar sympathetic chain results in a decrease in surface temperature of the leg and foot of the same side.

REFLEX AND GENERAL VASODILATATION

Vasodilatation of an extremity may be accomplished reflexly by the application of heat to another extremity or to another part of the body. For example, the lower extremities may be reflexly vasodilated by warming up a hand or by the application of heat to the upper abdomen. This may be a more simple means of improving the circulation in the lower extremity transitorily and is without trauma. Also, in those instances where therapeutic vasodilatation and anticoagulant therapy are necessary, needle punctures are contraindicated because an inadvertent needle puncture of a vessel may cause prolonged bleeding and become quite hazardous.

Chemical sympatholytic agents given systemically produce a general vasodilatation throughout the body. Hence, the dilatable areas in the uninvolved extremities draw upon the total blood volume more than usually and leave less blood available for the ischemic extremity. Furthermore, a general vasodilating agent reduces the systemic blood pressure, which, in turn, further reduces blood flow through the organically narrowed vessels. Hence, general vasodilators are actually contraindicated for the treatment of an organically ischemic extremity.

GANGRENE OF THE FOOT

Consideration of gangrene of the foot is approached as an entity somewhat separate from arterial insufficiency inasmuch as some patients with gangrene present evidence of an intact major arterial supply with pulsations present down to and including the dorsalis pedis and posterior tibial arteries. The involved

TABLE II

Differential Diagnosis

	Arteriosclerosis	*Thrombo-angiitis obliterans*	*Raynaud's phenomenon*
Age at Onset	50 years plus	20 to 30 years	Teens and 20's
Sex	Male and female	Male, rarely female	Usually female
Distribution	Lower and, occasionally, upper extremity	Upper and lower extremity	Usually upper extremity, bilateral, symmetrical
Course	Progressive or stationary	Exacerbations, and remissions with residua	Exacerbations and remissions with full recovery until late in course
Histopathology	Intimal fibrosis and thickening	Mononuclear inflammation of entire neurovascular bundle	Vasospasm of central origin
Gross Pathologic Anatomy	*Large* vessels mainly, such as aorta, iliacs, femoral & popliteal. Segmental occlusion frequent	*Medium-sized* vessels, as tibialis and peroneals. Short, segmental occlusions.	Arteriolar spasm
Precipitating Factors	Cold, stasis	Exposure to cold, tobacco	Emotion stress, exposure to cold
Pain	Mild to moderate	Severe	Severe
Complications	Thrombosis with occlusion. Gengrene requiring radical amputation.	Occlusions requiring conservative amputation	Gangrene only late

foot and leg may be as warm as, or warmer than, normal and with no critical temperature level drop. Other patients with the same amount of gangrene of the toes and foot have a cold leg and foot and no arterial pulsation beyond the thigh. The patients with gangrene associated with a warm foot and distal pulsations usually have diabetes mellitus, while those with the cool leg and absent pulsations have arteriosclerotic occlusion of a major vessel. Thus, gangrene of the lower extremity may be divided in general into the diabetic and arteriosclerotic types, with differing vascular patterns of patency and occlusion. A deficient blood supply is immediately responsible for a gangrenous toe in both types, consisting presumably in a thrombotic occlusion of the digital artery in the immediate region of the gangrene. The mechanism of production of this distal occlusion is basically quite different in the two types.

Diabetics have a lessened resistance to infection, as manifested by recurring boils or styes and frequent and persistent fungus infections such as monilial vaginitis and monilial intertrigo. Among the theories to account for this are the higher blood sugar values, a lack of complement, and decreased antibody formation. Hence, in a diabetic, with the pores of the skin normally containing many bacteria and fungi, an infection on or between the toes may readily occur. This infection extends into the soft tissues eventually to involve the artery with an inflammatory process which predisposes to thrombosis. The gangrene results from the local ischemia. In association with this, however, the major vessels above are usually not occluded—hence, the warm leg and foot with pulsations even down to the dorsalis pedis.

In arteriosclerotic gangrene, the occlusion of the digital artery in the region of the gangrene occurs also, but via a

circulatory mechanism instead of infection. In arteriosclerotic gangrene, a major vessel occlusion above, either in the iliac, femoral, or popliteal, is almost always present. This *per se* does not cause the gangrene inasmuch as many people with arteriosclerotic occlusion of these large vessels do not develop gangrene. Occlusion occurs also in those with only intermittent claudication. However, a major vessel occlusion above predisposes to the occlusion of the digital or metatarsal artery distally. This concept suggested itself during three surgical explorations of popliteal occlusions. In each instance the patent artery immediately proximal to the occlusion presented a strong, bounding, palpable, and distinctly visible pulse. Distal to the occluded segment, no pulsation of the artery could be seen or felt. Its patency was ascertained only by aspirations of bright red blood with syringe and needle. Thus, with occlusion of a major vessel in the extremity, the pulsatile character (grossly) of the blood flow is lost. Only rarely are collaterals so extensively developed that a gross pulsation is maintained after circumventing an occlusion. It appears probable that a single large diameter is necessary for maintaining or transmitting a gross pulsation. The mechanism for the occlusion of the small, distal vessel, therefore, is that of a grossly non-pulsatile blood flow—a relative stasis—predisposing to thrombosis in the small distal artery. The interval between the major vessel occlusion with its resultant pulseless blood flow and the eventual development of gangrene distally is quite variable. In one case in which both events were closely observed nearly three months ensued. Intervals in other instances are known to be much longer, and obviously, many old people succumb from other causes before this mechanism of a pulseless flow results in gangrene of the lower extremity.

Diabetic and arteriosclerotic gangrene may be further clinically classified according to the initial and/or subsequent development of *wet* or *dry* gangrene. In diabetic gangrene, the initial process is infection and, therefore, there is a wet gangrene from the onset. In the arteriosclerotic, with deficient blood supply, there is initially a dry gangrene. However, if ulceration of the dry gangrene occurs, infection supervenes, and the dry gangrene then becomes wet. This forms a basis for the treatment—primarily the treatment of infection in the diabetic and the prevention of infection (or its treatment) in addition to the treatment of a deficient (pulseless) blood supply in the arteriosclerotic.

Diabetics, however, do develop arteriosclerosis, and a patient with diabetes mellitus may develop an arteriosclerotic occlusion with a non-pulsating type of flow, and therefore originally present a dry gangrene. Nevertheless, a diabetic only occasionally develops arteriosclerotic dry gangrene in spite of the increased incidence of atherosclerosis in the disease.

THE FACTOR OF INFECTION

An important concept to be appreciated in the management of gangrene of the extremity is that of demarcation. Viable skin contiguous with the gangrene at first usually exhibits a hyperemic redness and an induration which gradually fade away from the gangrene. However, after a variable period the redness and induration disappear. Thus, with demarcation, the gangrenous portion is immediately contiguous with viable tissue which does not exhibit gross reactions to the dead part.

In the presence of infection, however, a *clear* line of demarcation does not develop inasmuch as the infection gradually subsides proximally. The infection locally leads to a proximal advancement of the gangrene, in part probably due to a bacterial infectious necrosis and also probably to infectious inflammatory involvement of the local vessels leading to their thrombotic occlusion. Furthermore, the same type of bacteria as are found on the infected gangrenous tissue of the toes or foot are frequently found, by culture, in the calf muscles. The greatest and most frequent hazard to life from a gangrenous foot or toe, however, is the systemic toxic effects of the infection.

A major problem in the treatment of gangrene, thus, is infection. In the diabetic, a prime consideration is the in-

fluence of the infection on the local advancement as well as upon subsequent systemic effects which may jeopardize the patient's life. Though antibiotic therapy is widely used, our experience is that infection of the toe proceeding to gangrene is very difficult to overcome. For possibly better results a routine culture from the gangrenous area is obtained, and sensitivity of the organisms found to the various antibiotics is determined. A complicating factor in this location, however, is that fungi are frequently present and may be responsible for the infection, and that fungi thrive under antibiotic therapy. Close co-operation with the bacteriologist is necessary.

The lower extremity lends itself to obtaining high tissue concentrations of therapeutic substances by slow femoral intra-arterial infusion at the groin. Penicillin may be given intra-arterially by slow drip through a needle inserted percutaneously into the femoral artery at the groin. To obtain a slow drip, the pressure in the flask (of saline and penicillin) is held at just above diastolic pressure. During systole the blood is seen to spurt upward into the glass needle adapter, and during diastole the drops of the solution enter the artery. With such slow infusion, adequate time appears available for capillary diffusion of a considerable quantity of the antibiotic, thus attaining an intense local concentration in the particular extremity.

These measures are applicable also to patients whose dry gangrene of arteriosclerotic origin has become wet because of superimposed infection. Because of the impaired blood flow there may be difficulty, however, in obtaining as high a level of antibiotic and other antibacterial substances.

LOCAL TREATMENT OF INFECTION

Local treatment for infection is equally important. First in importance is the prevention of infection in the dry gangrene of arteriosclerosis by the application of sterile, dry dressings. Wet dressings are avoided because of their macerating effect. Because of the antiseptic effect of alcohol and because its evaporation results in a dry dressing, alcohol application may be made. The principle of dry sterile, or sterile moist, evaporating (alcoholic) dressings applies to both the dry and the wet gangrene.

When the infection and toxic process become systemic, the patient frequently presents with a fever ranging as high as 104°F, an elevated non-protein nitrogen, and disorientation—and with a grave prognosis. However, by the application of ice packs to the gangrenous and infected foot and leg, this serious situation is usually overcome within 24 to 48 hours. The cooling decreases the metabolic rate of the tissues, of the various decomposing processes, and of the bacteria. The packing in ice is done with the premise that the leg is to be amputated after the general condition improves. Previously, with systemic manifestations, an emergency amputation was often done to remove the source of toxicity. However, the patient in this state was a poor surgical risk and the mortality rate was quite high. By applying ice packs to cool the extremity and improve the patient, the surgical risk is considerably improved. No emergency amputation is then necessary, as the patient's leg and foot may be kept in ice packs for several days before amputation.

By the same principle, the application of heat to a gangrenous foot is contraindicated. But even more important, practically, is the avoidance of heat to an extremity with impaired arterial circulation. The increase of oxygen need resulting from the increased metabolic rate, caused by the heating, is greater than the increased oxygen the hyperemia can supply in the presence of an impaired arterial circulation. Heat may be useful in treating an infection such as cellulitis of the foot and leg. Yet, when the arterial supply is impaired, the heat may precipitate gangrene. Hence, the application of heat to the lower extremity is contraindicated in the absence of a palpable dorsalis pedis pulse.

The decision for amputation is limited to the one admonition that conservatism in the level of amputation must be the watchword.

THE PYRAMIDAL TRACT

GEORGE CLARK, Ph.D.*

During the past fifteen years there has been much more research on the corticospinal motor system than during the remainder of the first half of this century. Among the problems extensively studied have been those of origin, composition, termination, and function while that of the pathway itself has received little attention. Some of the problems studied have been entirely new, but more have represented the use of new methods on old problems. In general, much of the work has simply shown that earlier studies were correct and that the textbook oversimplifications, current until recently, were not tenable. The account of the pyramidal tract as given by Barker[1] in 1899 is surprisingly modern.

Nothing of note has been added in the last fifty years as far as the pathway itself in the human is concerned, although some comparative work has been done. Douglas and Barr[2] noted that the course of the pyramidal tract in the rabbit furnishes an additional reason for separating that species from the Rodentia. Glees, Cole, Liddell, and Phillips[3] have recently removed the thumb area in a few *Macacca mulatta* and studied the resultant degeneration—a repetition of the old experiment of Mellus[4]. With the more exact Swank-Davenport method for the staining of degenerating myelinated fibers, they confirmed the lack of localization of the fibers within the brain stem that Mellus had stressed and, in addition, were able to trace the degeneration much farther caudally than was possible for Mellus. Indeed, they were able to demonstrate that descending fibers from the thumb area extend as far caudally as the lumbar enlargement. This certainly would not have been anticipated on the basis of a concept of the pyramidal tract such as was held by Fulton[5].

Until recently there has been little consideration of the number and the sizes of fibers in various nervous pathways, and it is only in the past decade that the pyramidal system has been shown to have a very complicated fiber spectrum for which there is as yet no explanation. Lassek and Rasmussen[6] and Lassek[7] have laboriously determined the number of fibers in the pyramids of several humans and a number of other species. In the human there are approximately one million fibers in each pyramid. Only 60% of these are myelinated and, of these, 89.6% are less than 5 $m\mu$ in diameter. 8.7% are from 5-10 $m\mu$ in diameter and only 1.7% are 11 $m\mu$ or larger in diameter.[8] Thus, approximately 95% of the fibers are less than 5 $m\mu$ in diameter and hence the average conduction velocity of the tract is very slow. Why a tract which has been presumed to be only for voluntary motion should have such a variety of fibers and so many slow conducting fibers is as yet only a matter for conjecture and cannot be explained. The fact that primates and carnivores have a much higher proportion of large fibers than rodents and ungulates[6,7] and that the exquisitely graceful porpoise apparently lacks a pyramidal tract[9], certainly gives no clue.

Although the number of fibers above the decussation is about one million, there are only one-fourth as many in the upper cervical region.[10] The ventral corticospinal pathway can account for only a few of these. The fate of the others is enigmatic. However, since the counts in the spinal cord were made on sections stained by the unreliable Bielshowsky method, this work should be repeated with modern silver techniques.

Having survived a period when the pyramidal tract was said to originate in area 4* of Brodmann, Barker's (1899) generalization has been shown to be cor-

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* The number designations of cortical areas proposed by Brodmann[11] are used throughout this review. They do serve to indicate approximate locations even though the areas themselves cannot be confirmed.

rect by several methods. Lassek[12] and Haggquist[13] have demonstrated that, after ablations limited as nearly as possible to area 4, almost 70% of the fibers in the homolateral pyramid of the macaque remain intact. Even after an ablation extending from the arcuate sulcus anteriorly to the postcentral sulcus posteriorly, 50% of the fibers remain.[12] It has been further shown that to insure complete degeneration of a pyramid it is necessary to almost completely ablate the homolateral cerebral cortex.[14] By Marchi methods, Peele[15] has shown that at least part of the fibers in the pyramids originate far caudally in the postcentral region. Much the same was shown, using another method, by Woolsey and Chang.[16] They stimulated the pyramids and recorded antidromic impulses over the convexity of the hemisphere. Only from the temporal, occipital, and the more anterior portions of the frontal lobes were potentials lacking. Their map of the origin of the pyramidal tract in the spider monkey is surprisingly similar to that of Horsley and Shaeffer.[17]

The same texts that limited the origin of the pyramidal tract to area 4 also claimed that the Betz cells were the cells of origin for this tract. Actual counts[18] of these elusive cells (they are defined only as giant pyramidal cells, and the question of when a large pyramidal cell becomes a giant cell is unanswered) have shown differences, but, in man,[19] there seem to be some 34,000—about twice the number of extremely large fibers in the pyramidal tract and about 3.4% of the total number of fibers in a pyramid. However, it is true that after area 4 lesions, most of these large fibers degenerated.[12]

Barker mentions that, in 1899, the question of the termination of the pyramidal tract was unsettled and that Von Monakow[20] was insisting that the fibers did not end on anterior horn cells but rather on internuncial cells near and in the posterior horn. Although Hoff and Hoff[21], who studied degenerative changes in terminals of the pyramidal tract, corroborated the opinion of von Monakow, texts continued to state that the pyramidal tract fibers did end on anterior horn calls until sometime after Lloyd's[22] oscillographic study of this question. He found no evidence for pyramidal tract fibers ending directly on anterior horn cells but did obtain excellent records which amply demonstrated the ending of such fibers in several portions of the posterior horn.

Damage to the pyramidal tract has long been said to result in a paralysis with spasticity, hyperactive deep reflexes, loss of superficial reflexes, and the appearance of abnormal reflexes. In this respect, Lassek[23-28], in a series of papers, has brought forth surprising data. For a number of years he collected material in an attempt to correlate changes in the pyramids with clinical findings. Since none of these cases were his own, he had to rely on case histories which, in a measure, limited his results. However, he reported that hemiparesis or hemiplegia can occur with little or no evidence of destruction of the fibers of the pyramidal tract. Of 106 cases of cerebrovascular disease, all of which had varying amounts of motor findings (55 cases of hemiplegia, 19 of hemiparesis and 32 with paralysis, loss of muscular power, limping or weakness), there was complete destruction of the pyramidal tract in only 7, while in 63 there was no overt evidence of a degenerative process. These findings are similar to others he collected from three neurological journals. He selected 1,600 consecutive cases of pyramidal tract syndromes where a unilateral or bilateral Babinski sign was reported. In only 19.6% of these were other pathological reflexes mentioned.

The following table is a summary of these cases:

Positive Babinski sign	1,600
Somatic motor deficit	1,376
Hyperactive patellar reflex	984
Absence of superficial reflexes	628
Spasticity	584
Ankle clonus	400
Hypoactive knee jerk	209
Absence of cremasteric reflex	96
Flaccidity	87
Patellar clonus	70

Lassek has also stressed that a Babinski sign may be elicited in a small percentage of persons with no other mani-

festation of a neurological disorder and that a temporary Babinski sign is seen in a variety of conditions, such as severe exertion, hypoglycemia, deep sleep, *etc.* These reports are difficult to assess. At the very least, they indicate a real need for investigation, but it is doubtful that they detract greatly from the clinical value of these tests.

These summaries of Lassek, however, do throw some doubt on the relationship between pyramidal tract lesions and spasticity, and do lend credence to theories, such as those of Magoun and Rhines[29], in which spasticity is considered an extrapyramidal deficiency. The theory of Magoun and Rhines is simple, teachable, and seems to explain so much that it has received wide attention. However, there are discrepancies which make it necessary to reject the theory. First, let us summarize the theory and then, discuss these discrepancies. According to Magoun and Rhines[29], spasticity is basically the result of interruption of inhibitory influences on anterior horn cells in the presence of an active facilitatory outflow which leaves the stretch reflexes unchecked. These inhibitory influences take origin in 4s, an area lying between areas 4 and 6. From 4s, a pathway extends via the internal capsule to the bulbar inhibitory area. This is a portion of the medial reticular formation extending from near the lower border of the inferior olive to about the midpontile region. From here, a pathway passes mainly in the ventral part of the lateral funiculus to end probably on internuncial cells which, in turn, send impulses to the anterior horn cells. "A patho-physiological consequence of injury to this inhibitory system at any point is exaggeration of spinal stretch-reflexes. Whether tested by clinical examination or electromyography, this exaggeration of reflexes is manifested by increased resistance to manipulation, with augmented contraction both of the stretched muscle and, reflexly, by secondary stretch, of its antagonist; by low threshold, brisk and irradiating deep reflexes; and by clonus and other unusual synchronization and repetition of motor activity-alterations collectively described as spasticity."[29] Much of the remainder of the reticular formation of the brain stem also sends descending fibers, but these are facilitatory in character. Stimulation of this region will increase the extent of force of a cortically or rereflexly induced movement. Similarly, appropriate stimulation of 4s or of the bulbar inhibitory area will inhibit a cortically induced motor response and conversely, a lesion at any point which interrupts the transmission of the inhibitory impulses to the bulbar inhibitory area will result in spasticity, since the latter is activated only by the cerebral cortex. The facilitatory area, on the other hand, receives collaterals from the great ascending sensory systems and is active in the absence of the cortex. Magoun and Rhines[29] consider the spontaneous low voltage potentials which Adrian and Moruzzi[3] recorded from the pyramids as facilitatory in nature and their interruption (in the presence of an intact inhibitory pathway) to form the basis for the hypotonia which has been said to result from lesions confined to area 4[31], section of the cerebral peduncles[32], sections of the pyramids[33, 34], or sections of the lateral corticospinal pathway[35]. The above includes some experimental data and much theory. What is fancy and what is fact?

The basis for this theory is primarily the experimental studies on the bulbar inhibitory and facilitatory areas to which is added the studies on suppression and reports on the effects of damage to the pyramidal system in experimental animals. It must be stressed that the theory can be no more correct than the work on which it is based. The theory must either be discarded or modified to the same extent that any of its three sources are shown to be incorrect. The experiments of Magoun and his co-workers seem to have established the existence of the bulbar inhibitory and the facilitatory areas, but recent work has cast considerable doubt on the specificity of suppressor areas and on the results which have been said to follow damage to the pyramidal system. Magoun and Rhines[29] accept as proved the existence of specific suppressor areas in the cerebral cortex and the specific activities that have been

attributed to them. As stated by McCulloch[36] and by Garol and Bucy[37], there are five suppressor bands. Appropriate stimulation of any of these suppressor bands will produce: (1) a wave of decreased electrical activity of the cortex which passes in all directions from the point stimulated; (2) an increase in threshold of area 4; (3) a failure to produce a peripheral motor response by cortical stimulation; (4) a decrease of existing muscular tension throughout the body; (5) a holding in abeyance of a motor after-discharge induced by stimulation of area 4. Recent work[38-44], makes necessary a complete re-evaluation of these claims. The decrease in electrical activity of the cortex was said by McCulloch[36] to involve a circuit from suppressor bands to the caudate nucleus, to the thalamus and back to the cortex. The work of Sloan and Jasper[42] demonstrated that the experiments on which the circuit was based were not conclusive. Sloan and Jasper[42] have fully demonstrated that, although a shallow cut does not limit the propagation of the depression, a thin strip of some insulating material placed in the cut halts the wavelike spread of decreased electrical activity. Thus, neural contiguity and not neural continuity is required and the subcortical pathway described by McCulloch[36] is not essential. In addition, this response may be elicited from wide areas of the cortex—the spreading depression is not limited to the suppressor areas. The time relations of the inhibition of a cortically induced motor response and the increase in threshold of area 4 are the same as those of the spreading depression of electrical activity of the cortex. In each case the latency is measured in minutes with some variation due to the depth of anesthesia and to the condition of the animal. As Kaada[44] suggested, all three are probably different aspects of the same phenomenon and, despite the protestations of McCulloch[45], this phenomenon is probably identical with what Leao[46] described as spreading depression—a process elicitable from almost all the cortex.

There remain two facets of suppression: an inhibition of postural tone and the holding in abeyance of a motor after-discharge. The first of these has been elicited from many regions of the cortex[38, 47, 48]. It is noteworthy that those who have reported this phenomenon in unanesthetized animals[38, 48], failed to elicit this response from the frontal eye-fields (area 8s) or from points which, on the basis of the maps of McCulloch[36], would lie in 4s; but they did obtain a reduction in tone from a few locations with a stimulus subliminal for a motor response. Even when 24s, the most powerful of the suppressor areas[49], was stimulated in unanesthetized animals[40, 41, 44] no loss of muscular tone could be discerned. Kaada[44] has reported that, "a holding in abeyance of a motor after-discharge elicited by stimulation of any focus in the sensory motor cortex" may be obtained from a variety of locations. It is important to note that among the points from which he elicited this response were the tip of the temporal lobe and the posterior orbital region, which are rather remote from suppressor bands. Thus, not one of the five facets of suppression is peculiar to the suppressor areas, including all the effects common to stimulation of the bulbar inhibitory area and the suppressor bands. There remains no functional link specific to the so-called suppressor areas and the bulbar inhibitory area. No response elicitable from the bulbar inhibitory area is also elicitable *only* from the supposed origin of the corticobulbar inhibitory area pathway.

If the responses which were used to delimit the suppressor areas may be elicited from wide areas of the cortex, the concept of suppressor bands is erroneous and should be discarded. It is, thus, not surprising that Lashley and Clark[50] and Bailey and von Bonin[51] in their studies of cortical architectonics have failed to find histological evidence for their existence. Similarly, Snider and Eldred[52] find nothing in the way of cerebellar connections to distinguish 4s and 6 although it must be mentioned that they located 4s only on its supposed relation to the "superior precentral dimple".

However, in one respect 4s has been said to differ from the other so-called suppressor bands. Ablation of 4s has been

said to result in spasticity.[53] If this is correct, and if 4s is the only cortical area whose ablation results in spasticity, the theory could be salvaged. The work of Denny-Brown and Botterell[54], which will be discussed in the next section, shows quite clearly that, even in this respect, 4s cannot be upheld as a functional unit.

Magoun and Rhines[29], as has been said before, consider spasticity as due to interruption of the inhibitory pathway while the facilitatory pathway is intact. They discuss the pyramidal pathway as one of the facilitatory pathways. They apparently believe that ample evidence for this is afforded by the reports of (a) Fulton and his associates[53] that removal of area 4 results in a flaccid paralysis and that only when the lesion is extended anteriorly, *i.e.* so as to include 4s, does the paralysis become spastic and (b) that section of the pyramidal tract at various levels (cerebral peduncles[32]; pyramids[33, 34]; lateral corticospinal tract[32]) results in hypotonia. There is, however, serious doubt as to the validity of at least two of these reports—the only two for which there are now added data. Denny-Brown and Botterell[54] have recently reported in detail on a series of ablations of the motor cortex. In contrast to the reports of Fulton and associates[53], they failed to find a consistent relationship *only* between 4s ablations and spasticity. On the contrary, spasticity may just as well result from sparing the caudal portion of area 4. Their important finding is that many different partial lesions of area 4 may lead to spasticity. Since area 4 itself does not project onto the bulbar inhibitory area[57], this finding is not consistent with the theory of Magoun and Rhines.[29] There have been no subsequent reports on cerebral peduncle section, but it is important to note that according to the theory a hypotonicity from cerebral peduncle section can only result if the inhibitory pathway is intact. There are new data available on the effect of section of the pyramids. Denny-Brown[55] reports that, in his hands, such an operation on the monkey results in a hemiplegic type of rigidity and Liddell and Phillips[56] make the devastating statement that, in the cat, "a crossed extensor hypertonia is the invariable consequence of *uncomplicated* section of a medullary pyramid". The obvious conclusion is that, contrary to the theory of Magoun and Rhines[29], hypotonicity does not result from section of the pyramids.

The supposed pathway from 4s to the bulbar inhibitory area has been sketched by Magoun and Rhines[29]. From 4s, it is said to pass to the internal capsule, then to the cerebral peduncles, which it leaves in the lower mesencephalon to enter the pontile tegmentum and ends in the bulbar inhibitory area. The pathway must lie in the most medial portion of the cerebral peduncles for this region was spared in the cerebral peduncle sections of Cannon, Magoun and Windle[32]. These preparations were said to be hypotonic and this condition can only result, according to the Magoun and Rhines[29] theory, if the 4s bulbar inhibitory pathway is intact. However, at the lower end of the mesencephalon the pathway leaves the pyramidal tract to enter the pontile tegmentum. At this level it must diverge some distance from the pyramidal tract, as section of the cerebral peduncles at that level did not interrupt the transmission of strychnine spikes to the bulbar inhibitory area.[57] Magoun and Rhines[29] cite the work of Verhaart and Kennard[58], and of Hines[59] as proving the projection of the pathway to the medial pontile tegmentum. Both of these demonstrated, by the Marchi method, that degeneration was found in this region of the brain stem after lesions in 4s. However, Hines[59] also reported that degeneration could also be followed in the pyramidal tract into the spinal cord. This latter conclusion is consistent with the theory of Magoun and Rhines[29] only if the lesions made by Hines[60] were not confined to 4s. It should be pointed out, however, that Hines[60] was the first to recognize such an area. Finally, although the 4s bulbar inhibitory area pathway must diverge from the pyramidal tract, it must remain in close association with it. At the last meeting of the American Association of Anatomists, Magoun, in the discussion of a paper by Scheibel[61], stated that the work of Scheibel represented an anatomical confirmation of the physiological studies on

the efferent fibers to the brain stem reticular formation. With Golgi studies, Scheibel[61] had demonstrated that the brain stem reticular formation had two sources of afferents. The lateral portion (Magoun's facilitatory area) receives fibers from the region of the great ascending sensory systems while the medial portion (Magoun's inhibitory area) receives fibers from the region of the pyramidal tract. In this medial region, the 4s inhibitory area must, then, lie adjacent to the pyramids and yet must not have been included in the unwanted extensions of the lesions which produced hypotonicity in the cats with complicated sections of the pyramids[56], and presumably in the cats and monkeys of Tower[33, 34].

These discrepancies may be summarized as follows. Although the Magoun and Rhines[29]theory accepts the concepts of suppression, as proved, and is based on these concepts, recent work has shown that none of the responses which were used to delimit the supressor bands are elicitable *only* from the suppressor bands. In fact, the concept should be discarded. Spasticity, which, according to the theory of Magoun and Rhines, can only result from damage to 4s or the 4s bulbar inhibitory area pathway, can be produced by damage to other portions of area 4 which do not project to the bulbar inhibitory area. Finally, there are discrepancies in the pathway itself which are hard to reconcile.

Space does not permit more than a final general objection, although others could be listed. Any theory purporting to explain spasticity must, of necessity, also explain the laterality usually shown by this phenomenon. Hemiplegia is much more common than paraplegia. According to McCulloch, Graf, and Magoun[57], 4s projects to both sides of the bulbar inhibitory area and according to Magoun and Rhines[29], the bulbar inhibitory area likewise acts bilaterally. There is no provision in the theory, nor can one be attempted from their data, to account for a unilateral spasticity.

The only conclusion possible seems to be that the spasticity theory of Magoun and Rhines is untenable in its present form and that its wide acceptance is unfortunate.

SUMMARY

The account of the pyramidal tract as given by Barker (1899) is consistent with the details that have been added since that time. In particular, his mention that the tract has origin over a wide expanse of the cerebral cortex and his recognition of the controversy current at that time, as to whether the termination was on anterior horn cells or on internuncial cells, must be commended. Recent work has amply confirmed the wide origin of this pathway and has shown that most, if not all, fibers end on internuncial cells. The wide fiber spectrum of the pyramidal tract was not suspected by Barker, nor did he suspect the fact that so many of the fibers are of such small caliber. Current theories offer no explanation for these findings. Although the reports of Tower that, in the cat and the monkey, section of the pyramidal tract results in hypotonicity, were widely accepted, it now appears that such acceptance was overhasty and that, on the contrary, hypertonia results from such an insult. The spasticity theory of Magoun and Rhines is untenable.

REFERENCES

1. Barker, L. F., The Nervous System and its constituent neurons., 1899 (reprinted by Stechert and Co., New York, 1909.)
2. Douglas, A. S. and Barr, M. L., Rev. Can. de biol., *9*:118, 1950.
3. Glees, P., Cole, J., Liddell, E. G. T., and Phillips, C. G., Arch. F. Psychiat. u. Zeitsch. Neurol., *185*:675, 1950.
4. Mellus, E. L., J. nerv. ment. Dis., *26*:197, 1899.
5. Fulton, J. F., Physiology of the nervous system., London, Oxford U. Press, 1938.
6. Lassek, A. M. and Rasmussen, G. L., J. comp. Neurol., *72*:417, 1940.
7. Lassek, A. M., J. comp. Neurol., *77*:399, 1940.
8. Lassek, A. M., J. Comp. Neurol., *76*:217, 1942.
9. Lassek, A. M. and Clark, G., unpublished observations.
10. Weil, A. and Lassek, A. M., Arch. Neurol. Psychiat., Chicago, *22*:495, 1929.
11. Brodmann, K., Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues., J. A. Barth, Leipzig., 1909.

12. Lassek, A. M., J. nerv. ment. Dis., *95*:721, 1942.
13. Haggquist, G., Acta psychiat. et neurol., *12*:457, 1937.
14. Lassek, A. M. and Evans, J. P., J. comp. Neurol., *84*:11, 1946.
15. Peele, T. L., J. comp. Neur., *77*:693, 1942.
16. Woolsey, C. N. and Chang, H. T., Res. Publ. Ass. nerv. men. Dis., *27*:146, 1948.
17. Horsley, V. and Schaefer, E. A., Phil. Tr. Lond., 1888, cited by Barker[1].
18. Walshe, F. M. R., Brain, *65*:409, 1942.
19. Lassek, A. M., Arch. Neurol. Psychiat., *44*: 718, 1940.
20. von Monakow, C., Arch. f. Psychiat. u. Nervenkr., *28*:1, 1895, cited by Barker[1].
21. Hoff, E. C. and Hoff, H. E., Brain, *57*:454, 1934.
22. Lloyd, D. P. C., J. Neurophysiol., *6*:316, 1941.
23. Lassek, A. M., J. S. C. Med. Ass., *38*:243, 1942.
24. Lassek, A. M., Arch. Neurol. Psychiat., *52*: 484, 1944.
25. Lassek, A. M., J. Neuropath. exp. Neurol., *3*:189, 1944.
26. Lassek, A. M., Arch. Neurol. Psychiat., *53*: 375, 1945.
27. Lassek, A. M., Arch. Neurol. Psychiat., *54*: 339, 1945.
28. Lassek, A. M., J. S. C. Med. Ass., *44*:78, 1948.
29. Magoun, H. W. and Rhines, R., Spasticity, the stretch-reflex and extrapyramidal systems. C. C. Thomas, Springfield, 1947.
30. Adrian, E. D. and Moruzzi, G., J. Physiol., *97*:153, 1939.
31. Fulton, J. F., New England J. Med., *17*:1017, 1937.
32. Cannon, B. W., Magoun, H. W., and Windle, W. F., J. Neurophysiol., *7*:425, 1944.
33. Tower, S. S., Brain, *59*:408, 1936.
34. Tower, S. S., Brain, *63*:36, 1940.
35. Cannon, B. W., Beaton, L. E., and Ranson, S. W., Jr., J. Neurophysiol., *6*:425, 1943.
36. McCulloch, W. S., Physiol. Rev., *24*:390, 1944.
37. Garol, H. W. and Bucy, P., Arch. Neurol. Psychiat., *51*:528, 1944.
38. Clark, George and Ward, J. W., Brain, *71*: 332, 1948.
39. Clark, George and Ward, J. W., Amer. J. Psysiol., *158*:474, 1949.
40. Clark, George, Chow, K. L., Gillespie, C. C., and Klotz, D. A., J. Neurophysiol., *12*:459, 1948.
41. Goldzband, M. G., Goldberg, S. E., and Clark, G., Amer. J. Physiol., *167*:127, 1951.
42. Sloan, N. and Jasper, H., E.E.G. Clin. Neurophysiol., 2:317, 1950.
43. Marshall, W. H., Hanna, C., and Barnard, G., E.E.G. Clin. Neurophysiol., 2:177, 1950.
44. Kaada, B. R., Acta Psysiol. Scand., vol. 23, suppl. 83, 1951.
45. McCulloch, W. S., E.E.G. Clin. Neurophysiol., 1:19, 1949.
46. Leao, A. A. P., J. Neurophysiol. 7:359, 1944.
47. Tower, S. S., Brain, *58*:238, 1935.
48. Ward, J. W., J. Neurophysiol., *1*:463, 1938.
49. Ward, Jr., A. A., J. Neurophysiol., *11*:13, 1948.
50. Lashley, K. S. and Clark, G., J. comp. Neurol., *85*:223, 1946.
51. Bailey, P., and von Bonin, G., Ill. mon. med. sci., v. 6, no. 1-2, 1951.
52. Snider, R. S. and Eldred, E., J. Neurophysiol., *15*:27, 1952.
53. Fulton, J. F., Physiology of the nervous system., Oxford U. Press, London, 1943. (2nd ed.)
54. Denny-Brown, D. and Botterell, E. H., Res. Publ. Ass. nerv. ment. Dis., *27*:235, 1948
55. Denny-Brown, D., J. nerv. & ment. Dis., *112*:1, 1950.
56. Liddell, E. G. T. and Phillips, C. G., Brain, *69*:264, 1946.
57. McCulloch, W. S., Graf, C., and Magoun, H. W., J. Neurophysiol., *9*:127, 1946.
58. Verhaart, W. J. C. and Kennard, M. A., J. Anat., *74*:239, 1940.
59. Hines, M., Biol. Rev., *18*:1, 1943.
60. Hines, M., Amer. J. Physiol., *116*:76, 1936.
61 Scheibel, A. B., Anat. Rec., *109*:345, 1951.

THE GENESIS OF ABNORMAL BEHAVIOR *

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BASIC PRINCIPLES

In all likelihood, man's behavior has been a topic of interest ever since prehistoric times. In order to explain behavior which seemed to have its origin outside of the individual, he attributed such actions to agents outside of his control "possessed of the devil." The concept of lunatic influences of the moon on human behavior are examples of such formulations. This type of thinking is manifest in our present day concepts of mental disease, in such etiologic explanations for the cough, fever, leukocytosis of pneumonia, as is evident in the expression "catching pneumonia." At other times, stress was laid upon the hereditary nature of the genesis of man's behavior and emphasis placed on the Original Sin as a pre-determining factor of man's disturbed behavior. As in all other diseases, the fundamental factors in mental disease are the interrelationship between the subject or patient, and the influences brought to bear on the patient from the time of the fertilization of the egg by the sperm. The concept of man as an "intelligent animal trying to secure the greatest satisfaction for his own desires in an extremely complex social and physical milieu," is making more and more headway as a basis for understanding human behavior. This concept has been very clearly expressed in a theory described as a biodynamic explanation of human behavior (Masserman). This theory is based upon certain assumptions which are obtained from a study of psychoanalysis, psychology, anthropology and the social sciences. It is axiomatic that adequate consideration must be given to the needs for homeostasis in any theory of behavior. Activity involves disbalance in homeostasis in terms of the balance or in the equilibrium established between the organism and the environment, and that homeostasis is constantly being sought by the organism.

The biodynamic viewpoint of behavior offers a theory based on studies which encompass the entire phylogenetic and ontogenetic development of the individual and the field in which the behavior occurred. The following principles, basic in the understanding of human behavior, are derived as a result of such a study:

1. Behavior is motivated by the needs of the organism and is directed at satisfying those needs.
2. Behavior is dependent upon and adaptive to the total environment of the individual. The organism utilizes its total capacities and previous experiences in making the adaptation.
3. Behavior becomes deviated and disconnected under stress leading to the seeking of substitutive satisfactions involving less stress.
4. When in a given milieu two or more motivations come in conflict, anxiety mounts and behavior becomes hesitant, vacillating, erratic and poorly adaptive (neurotic or regressively substitutive), symbolic and regressive (psychotic).

In the interplay between the forces inherent in the organism and the environmental forces which hinder the development and expression of the inherent drives, the central nervous system is the integrating and coordinating system of the body and, thereby, the chief regulator of stability and the homeostasis of the organism in its totality. It must through its sensory end organs perceive stimuli externally and from within: it must evaluate, integrate and respond to them. The appreciation and awareness of external or internal stimuli gives to the organism the quality of excitement or the calling of the organism into action.

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Excitement is dissipated in discharge through activity; it may be bound or dammed up; or a combination of partial discharge and partial binding may occur. Whenever the influx of excitement is too intense to permit the individual to cope with the intensity of the bombardment, an emergency state exists.

Determinants of Abnormal Behavior

To understand abnormal behavior in man, one must consider those influences which are inherent in the organism, which contribute to the development and growth of the individual through infancy, childhood, adolescence and maturity. One must consider the personality structure which is determined by the need to mold, set or get certain patterns of reaction to conflict between the instinctual drives and frustrating environmental influences, so that the integrity of the organism is maintained while yet allowing a maximal amount of gratification for the individual.

A. *Hereditary factors*

Certainly there is an extensive literature which deals with the hereditary factors in the determination of behavior. And to some extent, deviations in behavior may be related to the particular genetic makeup of the individual. Not only is structure largely determined by gene transmission, but according to Freud, Jung and others, certain inherited mental patterns of reactivity (archetypes) are likewise transmitted. However, the more frequent opinion is that the milieu is more important to determine the deviant behavior of the individual than the hereditary factors.

B. *Developmental factors*

The influences within the first years of life which contribute to the development of the personality are of such great significance that one must review the important factors in infantile development to comprehend the genesis of behavior.

The human infant is more helpless than other mammals at birth and is subject to an influx of stimuli which he cannot master. There are at first undifferentiated reactions by the organism as a whole to external stimuli. The origin of ego functions, the taking in of the external world, mastery of the motor apparatus and ability to bind the excitation produced by external and internal stimuli lies in an attempt to deal with the unpleasureable feeling produced by the influx of excitation from without and from within by discharge of tension or avoidance of pain. Conscious awareness of any sort seems to be related to states of greater or lesser tension.

(a) *Dependent needs and oral erotic gratification*

Earliest experiences of the infant center around incorporation of objects in the external world. Sucking at the breast is the major source of gratification. Reality recognition in terms of establishing that which is object and that which is self has its foundation in being able to judge whether something helps to gain satisfaction or whether it raises tension, whether one should swallow or spit out that which is taken into the mouth. The earliest experiences of the infant, as one would expect, are primitive and undifferentiated. With the development of a concept of adults' omnipotence and that adults supply love or remove it, there is established obedience to authority through the threat of removal of supplies of love or affection. The needs to be loved and to obey have their origin in whole or in part in the helplessness of the infant and his dependence on parents for his major source of gratification and freedom from anxiety (oral gratification).

(b) *Development through mastery*

With the development of motility and a system of perception and motor expression, the infant tests out the environment and develops a certain mastery and sense of mastery of his surroundings. In so doing, he learns to supplant purposeful actions which require delayed judgment and choice for the total response to stimuli which are immediate and undifferentiated and characteristic of his earliest experiences. He can now begin to control and bind excitement and anticipate danger. In learning that instinctual urges are dangerous, he develops the ultimate basis for the development

of neuroses. With the introduction of words and language a further strengthening of the elements of the perceiving, integrating, motor components of the individual takes place in that choice, judgment and finer discrimination precede action. Out of the primitive undifferentiated organism, which cannot distinguish between self and object, parts and wholes, excitation from without and motor discharge, is developed a more effective organism through recognition of danger by objects from without and instinctual urges from within. Through the development of anxiety and fear and the ability to master the anxiety and fear through evaluation of and anticipation of the dangers from without and the control of the instinctual urges from within, logical thinking and reality testing are acquired. Logical thinking presupposes a strong ego that is capable of postponements, tolerant of tensions and ready to judge reality according to its experiences. Reaction, however, must not only be postponed but also curtailed and defenses are necessary to act as a bulwark against impulses which would endanger the organism. The defenses produced are a result of such factors.

(c) *Other developmental factors*

Just as incorporation of food is a focal point of development in the infant, one finds other areas in which a sharp focus is brought upon maturational factors which become of primary influence in development. These areas are being given here in outline, but emphasis should be given to the first two factors as important determinants of personality structure.

1. Bladder and bowel control
2. Genital primacy as an erogenous zone
3. Adolescence
4. Maturity and procreation
5. Climacterium
6. Senescence

The complex interrelationships of growth and maturation in the structural makeup of man with concomitant growth and maturation in the psyche and the resultant changes in adaptive capacity can only be mentioned. Certainly genetic, hormonal, enzymatic and other biochemical factors primarily determined by constitution, play an important role in the genesis of behavioral tendencies and patterns and, therefore, contribute to the development of abnormal behavior.

C. *The interaction of goal directed needs and environment as a behavioral determinant.*

(a) *The inner pushes of the organism*

Something should now be said about the nature of the drives, instincts and needs of the individual. They can in general be classified as those which aim at satisfying certain basic physical needs such as hunger, thirst, evacuation of excreta and breathing, and those which are related to sexual satisfactions. The source of these seemingly separate drives can, however, be traced to one common activity, that of relieving inner tension. Some special characteristics of the sexual drive need emphasis at this point. The sexual drive goes through phases of undifferentiated total sexuality which are partial instincts of the genitally oriented and climactically discharged genitality of "normal" adult sexuality. Oral, anal and other infantile genital organizations of sexual excitement show varying degrees of predominance, and tend to have a preponderance of possibility for arousing sexual feelings at any one of these zones during periods in which such zones are of prime importance in the development of the organism. The drives of the organism are directed at a goal or object through which satisfaction can be obtained and tension relieved.

Conflict exists as a manifestation of the inhibition and blocking of the drives seeking expression and being prevented from reaching the goal of satisfaction of freedom from tension.

(b) *The milieu*

The environment as an agent which determines abnormal behavior could be the basis of volumes of discussion. In brief, some of the more important considerations as they affect the develop-

ment of abnormal behavior are given below. The inner needs of the organism cannot be met by the environment in terms of the absence of a suitable goal or object to give the necessary satisfactions to the individual. Many family, social and cultural factors impinge on the individual in such a way as to frustrate the goal seeking satisfactions sought by the organism. The frustrations vary in each family group, social group or cultural climate in many ways, and these variabilities alter the adaptive responses to frustration made by the organism. Variability in the time as well as in the nature of the frustrations produced by the environmental influences is important. Certainly the adaptation to the frustrations produced by the birth of a sibling will be different for a two-year-old child and a ten-year-old one. Not only is time an important element in determining influences on behavior by the total forces which go to make the milieu, but the place in which the organism experiences the frustrations may be a crucial factor. In essence, the what, the when and the where of the frustrating or permissive factors in environment are important. Another generality worthy of note is that the relationships established in the family circle—father, mother, siblings, are basic for all the attitudes and behavioral tendencies in interpersonal relationships with all other humans. These basic relationships establish the attitudes and behavioral tendencies with regard to love and hate, authority and permissiveness, submission and aggression, ambition and apathy.

It is to be remembered that the environment is not an unchangeable structure, but rather a complex set of circumstances, objects and activities which not only influence the individual but is constantly being changed by individuals and groups of individuals. There likewise is no sharp line of demarcation between that which is object or activity outside of the individual (environment) and that which constitutes the organism. Food becomes part of the individual when taken into the mouth. It is part of the milieu when on the table.

(c) *Possible responses in the interplay between the organism and the milieu*

The description of the inner pushes and the effects of environmental influences on such pushes suggests that these factors in behavioral tendencies are working in opposition to each other. Actually, there are several avenues of behavioral operation possible for the organism in the interplay of activity between the pushes and milieu. The major possibilities for activity are essentially these: (1) the environment may offer the proper object and circumstances for complete gratification of the drive with complete relief of tension, (2) partial gratification may occur with sufficient satisfaction and release of tension to maintain a reasonable degree of psychological homeostasis, (3) there may be substitutive objects and circumstances used for gratification which may be sufficient to maintain an economic balance, (4) blocking of the drive for satisfaction because of the dangers to the organism and the seeking of partial or substitute gratification which give some satisfaction but not enough to maintain good psychological balance, (5) blocking of the goal directed pushes of the individual without any partial or substitutive satisfaction.

The question of what determines the organism's failure in completing the activity which is goal directed and satisfaction seeking must be answered.

D. *The role of anxiety*

The blocking of goal directed behavior is explained as being determined by anxiety. Anxiety is the diffuse feeling of uneasiness and apprehension associated with certain visceromotor and skeletal tensions which has as its function the task of appraising the individual of the danger of an impending conflict. Basic in the understanding of abnormal behavioral tendencies is the appreciation of the role of anxiety. Anxiety is a response to a threat from within, and fear a response to a threat from without.

At first, all reactions are an expression of a response to external danger, but as the organism matures and experiences

it tends to develop a more economic adaptive reaction by shortening the distance between the threatening external object and self by the development of a self-governing control over the inner pushes. The self restriction is acquired by the incorporation within the organism of the attitudes of the family and the social group, so that punishment and loss of love are avoided and approval is obtained. These behavioral tendencies for the self-control of the instinctual activities of the individual have been given a structural position between the inner drives of the individual and the environment, and called the super ego. When such an adaptive pattern has been established, the super ego then acts as had the external objects, *e.g.* parents, which previously created anxiety through warning the organism of the dangers from the instinctual drives and from external forces.

Anxiety in the adult can, according to Anna Freud, be divided into super ego anxiety (the conscience of the individual), objective anxiety (fear), and instinctual anxiety (dread of the strength of the instincts). Anxiety also undergoes modification so that it may express itself in such feelings as guilt, shame and disgust. Since anxiety has as its function the appraising of the individual of the possibility of danger, it is a means of defense in that it permits a certain stepping back for evaluation of the danger involved in some situations. Anxiety may be so overwhelming that it is not possible for the individual to master the influx of tension or in some instances there is so much of the organism's adaptive capacity bound into dealing with previous conflict that even minor degrees of increased tension may produce a psychological disbalance with confusion, fragmentation, and poorly integrated responses. Anxiety, fear, guilt, shame and disgust are developed as adaptive patterns to avoid danger either from self-punishing consciences or external objects. They have developed through painful experiences which the individual wishes to avoid re-experiencing. However, the warning signals are in themselves a source of discomfort and defensive measures in the nature of adaptive behavior directed against experiencing the discomfort of the warning signs of the affect are developed.

E. *Defense adaptations—behavioral responses in the avoidance of tension*

Thus far, the thesis of a disturbed psychological economy produced by the need for gratification of the organism and the frustration of those needs by the factors that represent the total environment has been described. Anxiety, fear and certain anxiety substitutes express a need to protect the individual against the possible dangers created by the pushes of the individual against a non-responsive environment. But the inner urges are constantly being mobilized and seeking expression. This constant drive by the organism to gratify its needs in goal directed behavior in a milieu which does not sanction the free expression of such drives leads to conflict since the ungratified drive and the anxiety created are experienced as unpleasurable and something of which the organism wishes to rid itself. The need for adaptive behavior which will protect the organism from anxiety and the creation of unpleasurable states may be summarized as stemming from the following factors:

(1) The outside world cannot always immediately be at hand. Desires cannot be gratified immediately as they are felt.

(2) Fear of retaliation from an outside world which the child perceives a similar violent force to its own.

(3) Danger in the outer world.

(4) The development of an inner force which judges the self, the drives, inner pushes, instincts and conflicts.

(5) The presence of conflicting drives simultaneously seeking expression.

The adaptive response of the organism in dealing with the above mentioned conflictual unpleasurable state, is the creation of behavioral tendencies which are in the nature of dampening the drives, avoidance of stimuli which will create tensions, partial substitutive and regressive expressions of the instinctual urges, and aggressive overcoming of the bar-

riers. These adaptive responses are described as the defenses of the individual.

A degree of stability is achieved through the defenses which for a time enables the individual to obtain a maximum of instinctual gratification with a minimum of anxiety. The intensity of and nature of such defense patterns of behavior are determined by the strength and the nature of the instinctual drives and the nature and the degree of restraint against such drives. Those defensive patterns which are found to be most successful for that organism will develop into certain fixed attitudes and character traits, which will give to the individual some of the set or mold by which we recognize him and refer to as his character.

There are certain defense reactions which enable the individual to cope with anxiety provoking situations as they occur. Others express a general reactivity, attitude, or character trait which becomes so much a part of the individual that his personality is described in terms of his defense attitude.

The more commonly described adaptive reactions of defense are the following:

(1) Repression — an involuntary repudiation.

(2) Supression—a voluntary repudiation.

(3) Resistance—a persistent wish not to recognize a feeling, motivation or desire.

(4) Rationalization — offering supposed explanations for behavior to hide the true meaning.

(5) Compensation and over-compensation—modes of behavior needed to avoid awareness of feelings of insecurity over ones own qualities or behavior.

(6) Reaction formation—the use of opposites for certain desires, feelings, *etc.*

(7) Displacement—shifting of emphasis.

(8) Projection — referring to others what is applicable to oneself.

(9) Identification.

(10) Denial of reality in phantasy and in word and act.

In addition to these individual methods of defense, one finds general patterns of protection, *e.g.* fixation, or maintaining a level of development instead of progressing to further maturation because the anxiety of coping with new problems created by further growth cannot be mastered. Having developed a pattern of behavior which may be considered more mature, the individual may find it desirable to regress to previous methods of adjustment rather than cope with new problems of adaptation. This mechanism of adaptation is known as regression.

References

1. Abraham Karl. The First Pregenital Stage of the Lerdo. Selected Papers, Hogarth Press, 1949.

2. Cannon, Walter B. Bodily Changes in Pain, Hunger, Fear and Rage.

3. Fenichel, Otto. Psychoanalytic Therapy of Neurosis, Wm. Norton and Co., New York, N. Y., 1945.

4. Freud, Anna. The Ego and Mechanisms of Defense. International Universities Press.

5. Freud, Sigmund. The Ego and the Id, Hogarth Press, London, 1948.

6. Freud, Sigmund. Instincts and Their Vicissitudes. Collected paper, Vol, IV.

7. Masserman, Jules. Behavior and Neuroses, University of Chicago Press, July 1946.

8. Masserman, Jules. Principles of Dynamic Psychiatry, W. B. Saunders, Philadelphia, 1946.

9. McHunt, V. Personality and the Behavior Disorders. Ronald Press, New York, 1945.

ADRENOCORTICOTROPIC HORMONE AND CORTISONE: THEIR ROLE IN ALLERGIC DISEASES

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Although much has been known about the anterior pituitary gland and its hormonal secretions, as well as the adrenal cortical hormones, it has only been about three years that great strides have been made in clarifying at least some of the important functions of these two glands of internal secretion. Hench and his associates had observed a peculiar phenomenon in patients suffering from rheumatoid arthritis. They noticed that such of their patients who became pregnant or developed jaundice had great relief from their arthritic symptomatology. This was felt to be due to an increased titer of biologically active steroids, probably derived from the adrenal cortex.

Kendall, by 1934, had isolated a number of crystalline compounds, which he lettered from A to F, and it was only a few years later that their chemical formulae were developed. One of this group, compound E, or cortisone acetate, was shown to have a definite effect on muscular activity and also some influence on carbohydrate metabolism. Compound E was found to be beneficial in the treatment of Addison's Disease and also demonstrated an ability to increase physiological resistance to stress, cold, and certain toxic substances. Laboratory attempts to prepare enough compound E for human use from glands, and finally by complete synthesis, were realized in 1947.

Since cortisone, when used over a span of time, causes the adrenal cortex to slow its normal output of this steroid, it was quite natural for investigators to attempt to find a substance which would continue to stimulate the adrenal cortex, and thus produce greater quantities of cortisone *in vivo*. This substance is, of course, adrenocorticotropic hormone (ACTH), which can be isolated from the anterior lobe of the pituitary gland. This hormone is known to be a protein of complex structure composed of peptids; however, at this writing, the exact chemical structure is unknown. A mixture of some of the polypeptides obtained from this protein has been shown to produce the same adrenal cortical stimulation as the original ACTH itself. There is, therefore, reason to believe that early synthesis of this hormone may soon be realized.

The anterior pituitary gland has three types of primary cells, the acidophiles, the basophiles, and the chromophobes. It is believed by most investigators that ACTH is produced by the acidophile cells. The release of adrenocorticotropic hormone is apparently brought about by stimulation of the adrenal medulla with associated release of epinephrine, which in turn activates the anterior pituitary gland. In the normal animal, under stress, the diencephalon is affected first and forms a center for transmitting stimuli from an autonomic source. The adrenal medulla is then activated, thus releasing a flow of epinephrine, which then stimulates the production and release of ACTH from the anterior pituitary.

Adrenocorticotropic hormone acts directly upon the adrenal cortex and stimulates the outflow of adrenal steroids, many of which are already known. There are produced numerous physiological changes according to the type of steroids which predominate. These latter are divided into three main classifications, depending on their mode and site of action, as follows:

1. *MINERALOCORTICOIDS* have a predominant effect on the electrolyte and fluid balance. Of this group, desoxycorticosterone is the most powerful. It is prepared synthetically, and occurs in the adrenal cortex in only very minute amounts. At present it is the only mineralocorticoid generally available for usage.

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Generally speaking, it causes retention of sodium and chloride and elimination of potassium by its direct effect on the kidneys. This steroid acts on the cells of the proximal convoluted tubules to stimulate reabsorption of chlorides. This in turn causes an increase in plasma and extracellular fluid volume with a decrease in the concentration of sodium and chlorides in the perspiration. The effects of desoxycorticosterone on water and electrolyte balance are practically the same as with cortisone, but the former is considered to be about thirty times as potent. The increased excretion of potassium, which is associated with the above, is not entirely understood, although it is believed that this alteration is probably due to a loss of intracellular potassium produced by protein breakdown and an associated displacement of intracellular potassium by sodium.

2. *GLUCOCORTICOIDS* are steroids which are primarily concerned with the intermediary metabolism of proteins and carbohydrates. All of the steroids in this group are structurally related and have an oxygen atom attached to the eleventh carbon atom. The best known members of this group are: Cortisone (Kendall's Compound E), 11-dehydrocorticosterone (Kendall's Compound A), corticosterone, and 17-hydroxycorticosterone (Kendalls' Compound F). Their functions are numerous, and the following comprise the major physiologic changes produced:

a) increase in conversion of endogenous protein to carbohydrates (gluconeogenesis).

b) increase in conversion of exogenous carbohydrate to glycogen.

c) more mobilization and utilization of fat with less oxidation of available carbohydrate, thereby sparing the latter.

d) increase in blood sugar level.

e) destruction of lymphocytes and eosinophils, as well as lymph nodes, and a neutrophilic leukocytosis.

f) depression of the function of the adrenal cortices and the thymus.

g) negative nitrogen balance, either due to increased protein catabolism or decreased protein anabolism, or both.

h) increase in antihyaluronidase activity.

i) increase resistance to certain types of stress, such as: infection, physical exertion, starvation, trauma, exposure to cold and other extremes of temperature, and the effects of certain drugs.

j) cortisone and compound F exert a mild effect on sodium, potassium, and water metabolism, but only about three percent as great as that of desoxycorticosterone (mineralocorticoid).

3. *"N" HORMONES* are adrenal cortical steroids which are essentially sex hormones and exhibit androgenic or anabolic activity. They are related to testosterone, but carry an oxygen molecule at the eleventh carbon atom. Adrenosterone and possibly estrone belong to this group. Adrenal androgens are held at least partially responsible for such secondary sex characteristics as growth of hair in the pubic and axillary areas, as well as on the extremities. Like testicular androgens, they cause retention of nitrogen, potassium, and sodium chloride. Their anabolic activity is weak.

Mode of action

Both ACTH and cortisone act as antiallergic and anti-inflammatory agents. The actual mode of action of both hormones is not yet clearly known, but it is believed that they act on the cellular level. They apparently protect the cell against toxic or injurious agents, and thus prevent destructive changes in and around the cell. From all known evidence, the damage is apparently reversible if the cell injury ceases short of necrosis.

Wedgewood and his co-workers were able to completely inhibit the development of glomerulonephritis (produced within fourteen days in rabbits by intravenous administration of bovine gamma globulin), by using ACTH intramuscularly for five days after injection of the antigen. Despite the failure of renal lesions to develop in the ACTH-treated animals, the antibody titers against the spe-

cific antigen and the drop in complement titers, apparently paralleling antigen-antibody union, proved to be identical with those in control groups. It appears, therefore, that ACTH exerts its protective influence through an agent acting directly on the cells of the renal parenchyma and not by interfering with antibody formation or with antigen-antibody interaction. Similar observations, using different antigens (horse serum and egg albumin), have been reported by other investigators.

Effect on Glands of Internal Secretion

ACTH and cortisones are known to cause structural and physiologic changes in many glands of internal secretion. Albright points out that all or nearly all patients with Cushing's syndrome have certain changes in the basophile cells described by Crooke. Golden and associates reported deaths following administration of ACTH in two patients with chronic glomerulonephritis, and noted morphologic changes in the anterior pituitary in both. These consisted of an increase in the total number of basophiles with Crooke's hyaline cytoplasmic changes and basophilic stippling of many of the chromophobes.

Forsham *et al.* report wide variations in the final response of the adrenal cortex in patients receiving ACTH for more than 48 hours. Functional regression took place within four days after discontinuing ACTH. Sprague *et al,* in their animal studies, noted that cortisone was able to maintain life in adrenalectomized animals, and that, in general, this hormone produced effects which compare with those described above. The major effect of ACTH is to stimulate the adrenal cortices to produce steroid hormones, some of which are closely allied to cortisone, and therefore produce a similar effect.

Cortisone and other allied adrenal hormones have an opposite effect on adrenal cortical activity and structure, as compared with ACTH. Exogenous cortisone apparently relieves the functioning adrenal cortex of its need to supply the endogenous hormone, and, over a protracted period, probably causes some atrophy of the adrenal cortex. Winter and his associates showed this to be true after prolonged administration of cortisone in rats, although the damage was reversible. Sprague observed that cortisone, in high dosage and over a prolonged period, induced most of the clinical and metabolic features of Cushing's syndrome (rounding of facial contour, hirsutism, acne, keratosis pilaris, muscle weakness, edema, amenorrhea, cutaneous striae, mental depression, impaired carbohydrate tolerance, negative nitrogen balance, increased excretion of corticosteroids in the urine, and hypochloremic, hypopotassemic alkalosis).

Thyroid function has been shown to be depressed by prolonged cortisone usage, with a decreased uptake of radioactive iodine and a decreased basal metabolic rate (reported by Sprague and his coworkers). Hardy noted also a decrease in protein-bound iodine.

Gonadal depression has been reported by numerous investigators, with amenorrhea a prominent feature.

TREATMENT of allergic diseases and other hypersensitive states has been greaetly enhanced since ACTH and cortisone have become available in sufficient quantity to satisfy patient requirements. Much has already been published, and more is yet to come, concerning the uses of these hormones. Not only their benefits, but also their dangers and relative contraindications will be proven as time goes on.

The laboratory studies of Rich and Gregory have suggested the relationship between the hypersensitive state and rheumatic disease. The relationship between adrenal cortical function and hypersensitivity has long been suspected. It was to be expected, therefore, that the effect of ACTH and cortisone on rheumatic disease would probably be duplicated in the hypersensitive state. This latter fact has been shown by numerous investigators, working independently.

De Vries reported a drop in circulating antibody titres following the use of ACTH in rabbits immunized with crystalline egg albumin, as differentiated from the work of Chase and associates, who reported a rise in the circulating antibody titres concomitant with a maximum drop in lymphocytes. However,

most investigators failed to find a significant change in the circulating antibodies. While Selye reports that both ACTH and cortisone inhibit anaphylactoid reactions in the rat following intraperitoneal administration of egg white, most other investigators find little or no effect on the anaphylactic reactions.

No alteration of skin sensitivity or skin reactions have been reported by many who have studied this problem, among them, Rose, Zeller, Samter, Rappaport, and Randolph.

Rose and associates reported a complete disappearance of urinary histamine in five of six patients with asthma during treatment with ACTH. However, adrenocorticotropic hormone does not influence the development of bronchospasm by histamine in asthmatic patients or in guinea pigs. ACTH is not believed to possess an antihistaminic effect.

Berthong *et al.* found visceral lesions of periarteritis nodosa in eighteen of twenty rabbits sensitized with horse serum, but only in five of twenty such animals which were treated with ACTH. It would appear that ACTH blocks the allergic process at the tissue level.

Insofar as infections or bacterial allergic reactions are concerned, tuberculosis has proven to be of great interest to many investigators. Generally, a marked exacerbation of all tuberculous lesions, upon administration of ACTH, has been the finding in laboratory as well as clinical studies. Freeman and associates have, however, observed amelioration of systemic symptoms in two patients. Several reports have appeared in the literature indicating a block in the Schwartzmann reaction by the use of ACTH in rabbits.

From the vast number of studies concerning ACTH and cortisone which have appeared in the literature in the past few years, it was natural that certain disease entities would be shown to yield dramatic results, that others would reveal little or no beneficial effects, and that many would fall somewhere between these two extremes. Forsham, in an excellent paper published in September 1951, has divided the diseases known to respond to ACTH and/or cortisone into several distinct groups, as follows:

HIGHLY INDICATED USES

Endocrine dysfunction (especially cortisone)
- a) adrenal cortical insufficiency
- b) panhypopituitarism
- c) adrenal androgenic hyperplasia
- d) idiopathic hypoglycemia

Collagen diseases
- a) acute rheumatic fever
- b) acute rheumatoid arthritis
- c) disseminated lupus erythematosus

Hypersensitiveness
- a) acute drug sensitivity
- b) contact dermatitis
- c) serum sickness
- d) exfoliative dermatitis
- e) acute hemolytic jaundice
- f) erythroblastosis fetalis

INDICATED USES
- a) chronic rheumatoid arthritis
- b) bronchial asthma
- c) acute gout
- d) acute dermatomyositis
- e) ulcerative colitis
- f) psoriasis
- g) surgery
- h) burns
- i) thrombophlebitis
- j) sarcoidosis
- k) chronic pulmonary inflammatory disease
- l) multiple myoloma (blast type)
- m) nephrotic edema
- n) pemphigus
- o) erythema nodosum

Acute inflammation and allergic diseases of the eye
- a) acute iritis
- b) acute keratitis
- c) acute uveitis
- d) acute choroiditis
- e) acute secondary glaucoma
- f) optic neuritis
- g) sympathetic ophthalmia

LIMITED VALUE
- a) multiple sclerosis
- b) scleroderma
- c) acute glomerulonephritis
- d) chronic atopic dermatitis
- e) leukemia

Only some of those conditions listed above, classified as allergic or hypersensitive state, will be considered in this report.

Bronchial Asthma

Both ACTH and cortisone have proven of benefit, especially in the relief of acute status asthmaticus, although chronic intractable bronchial asthma has also shown a favorable response. This has been shown in the work of Randolph, Zeller, Samter, Carryer, Feinberg and many others too numerous to mention. The use of intravenous ACTH has aided materially in interrupting the course of prolonged, otherwise unaided, status asthmaticus. For prolonged use, either intramuscular ACTH or cortisone, or oral cortisone acetate have proven to be of invaluable assistance.

Seasonal Pollinosis

Hay fever, of the seasonal variety, has shown a definite improvement following short course treatment with ACTH or cortisone. It has been observed by some investigators that when these hormones are used in hay fever subjects with accompanying asthma, the drugs will often yield quicker and more prolonged relief.

Atopic Dermatitis

Numerous reports of spectacular results in this disease have been made by many investigators. It was found by some that intramuscular injection of the hormone generally gave better results than did oral administration. However, in practically every instance, relapse occurred upon discontinuance of the drug.

Dermatomyositis

This disease, classified as one of the collagen group, responds only in part to ACTH or cortisone, depending on how far the pathology has progressed. Cellular infiltration, edema and induration apparently are reversible, according to Bunim. Thorn *et al.* are of the opinion that the acute inflammatory reactions and the destructive processes within the affected muscles are benefited by ACTH.

Lupus Erythematosus

Both good and disheartening results have been published concerning the use of ACTH or cortisone in patients with this disease, considered by some to be one of the collagen group. Thorn, Sulzberger, Brunsting, Haserick and many others have made valuable contributions to the therapy of this condition.

Serum Sickness

In this condition, the symptoms very often do not respond to the usual drugs, such as antihistaminics, baths, lotions, *etc.* ACTH or cortisone have shown remarkable ability in reversing the process, so that often within twenty-four hours, or less, complete cessation of symptoms occurs. Severe penicillin reactions, of the delayed onset type, are usually cured in 24 to 72 hours of treatment.

MODE OF ADMINISTRATION

ACTH

Adrenocorticotropic hormone may be administered in doses of 10 to 50 mg. intramuscularly every 6 to 8 hours, reducing the dosage and frequency of the injections as relief or complications develop. A long-acting preparation has recently become available, requiring an intramuscular injection every 12 or 24 hours. This procedure is especially adaptable for office use. The intravenous administration of 15 to 20 mg. in 5% glucose by very slow drip (8-12 hours), has shown promise of yielding more rapid results than the above methods. It is believed that the intravenous method is equivalent to giving five to ten times the amount of ACTH intramuscularly at six to eight hour intervals.

Cortisone

This hormone usually requires about two and one-half times the amount of ACTH to be equally effective by the intramuscular method. Usually 200 mg. is required, in divided doses, during the first twenty four hours. The oral 25 mg. tablet of cortisone acetate is a very convenient form of therapy in the ambulatory patient. Changing from ACTH or intramuscular cortisone should be done with caution, although no serious complications have ever been noted by the writer. Cortisone eye drops have proven of great benefit in allergic and in nontuberculous inflammatory diseases of the surface structures of the eye.

Generally speaking, either ACTH or cortisone may be chosen for starting treatment, although the latter is preferred if much edema is present, and the former is preferred if a marked nitrogen loss occurs before therapy is begun.

PRECAUTIONS

1. low salt diet
2. restrict fluids to 1500 c.c.
3. give 3 to 8 gm. enteric coated potassium chloride daily (prevents hypochloremic, hypopotassemic alkalosis)
4. insulin may be considered if the blood sugar rises above 125 mg.

CONTRAINDICATIONS

1. acute psychoses
2. active peptic ulcer
3. active tuberculosis and syphilis
4. hypertension (ACTH)
5. congestive heart failure due to mechanical defects
6. marked azotemia, with subacute or chronic glomerulonephritis
7. acute hemorrhagic tendencies

COMPLICATIONS

1. increased coagulability of the blood (unconfirmed)
2. increased pigmentation of skin
3. hirsutism and acne
4. striae, as in Cushing's syndrome
5. menstrual disturbances (amenorrhea)
6. mental depression
7. rupture of hollow viscus
8. constipation
9. drug reactions: as painful swellings at the site of injections, itching, urticaria, and angioneurotic edema.
10. anaphylactic shock was reported in only 3 of 1000 intramuscular injections of ACTH. Feinberg *et al.* reported such shock, with recovery by prompt treatment, in one patient who received 25 mg. ACTH. In such patients cortisone may be substituted.

SUMMARY

A resume of the physiology and pathologic physiology of the adrenocorticotropic hormone and cortisone is presented, emphasizing their effect on the adrenal gland and other structures. Their use in the treatment of allergic diseases and of other hypersensitive states, as well as complications, precautions, and contraindications, are presented.

It is the opinion of the author that these hormones have an important role in the treatment of hypersensitivity states, and also many other diseases. However, they can be dangerous if one fails to exercise all the necessary cautions in their usage. A careful study of their benefits as well as their possible side-effects must be made before prescribing them for therapeutic purposes. There is no doubt that more important data concerning their usage will reach the literature during the next few years to give us greater knowledge of the actions of all the glands of internal secretion.

BIBLIOGRAPHY

1. Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F.: Proc. Staff Meet. Mayo Clinic, *24*:277-297, 1949.
2. Thorn, G. W., et al.: New Eng. J. Med. *241*:529-537, 1949.
3. Sprague, R. G.: Am. J. Med. *10*:567, 1951.
4. Rose, B., et al.: Canad. M.A.J. *62*:6-9, 1950.
5. Randolph, T. G.: J. Lab. and Clin. Med. *34*:1896, 1949.
6. Sprague, R. G., Power, M. H., et al.: Arch. Int. Med. *85*:199, 1950.
7. Gordon, E. S., Kelsey, C., and Meyer, E. S.: Proc. Second Clin. ACTH Conference, Vol. 11.
8. Forsham, P. H.: Med. Clinics of North America, 1229, Sept. 1951.
9. Feinberg, S. M., et al.: Jour. All.: 22, 1951.
10. Derbes, V. J., and Weiss, T.: Quarterly Review All. and Applied Immunol. 5:No. 2, Jun. 1951.
11. Feinberg, S. M., Feinberg, A. R. Bigg, E.: J.A.M.A., 149, 1951.
12. Lever, W. F.: New England J. Med. *245*:359-363, Sept. 1951.
13. Brown, E. A.: Internat. Arch. of All. and Applied Immunology: 2, 1951, Fasc. 3.
14. Zeller, M., Randolph, T. G., and Rollins, J. P.: Ann. Allergy *8*:163-168, 1950.
15. Samter, M.: J. All. *21*:296, 1950.
16. Randolph, T. G., and Rollins, J. P.: Ann. Allergy *8*:149-162, 1950.
17. Randolph, T. G., and Rollins, J. P.: Ann. Allergy, *8*:169-174, 1950.
18. Carryer, H. M., et al.: J. Allergy, *21*:282, 1950.
19. Carryer, H. M., et al.: Proc. Staff Meet. Mayo Clinic, *25*:482-485, 1950.
20. DeVries, J. A.: J. Immunol., *65*:1-5, 1950.
21. Thorn, G. W.: New Eng. J. Med. *242*:783-793, 1950.
22. Irons, E. N., et al.: J.A.M.A. *145*:861-869, 1951.
23. Herschfus, J. A., et al.: Bull. New England M. Center. *12*:139-143, 1950.
24. Stefanini, M., et al.: J.A.M.A. *144*:1372-1374, 1950.
25. Downing, J. G.: New England J. Med. *246*: 56-65, and 94-101, 1952.

CLINICOPATHOLOGIC CONFERENCE

Presented at Mount Sinai Hospital, Chicago, Ill.

Dr. N. I. Fox, Chairman. Dr. I. Davidsohn, Secretary.

Abstracted by Dr. A. Oyamada

This 43-year-old white male, a liquor clerk, was admitted to Mount Sinai Hospital on August 10, 1951, because of the recurrence of a productive cough for the past six weeks. For twelve years, considerable cough with marked expectoration had been present, diagnosed as a bronchitis. This cough had gradually improved; then it became worse six weeks ago. The cough was now continuous, producing one-half cup of yellowish material per day, free of blood, and was associated with a pressing, choking chest pain, localized in the parasternal areas and right shoulder, and with lumbosacral pain. Dyspnea, orthopnea, generalized weakness and a weight loss of seven pounds were other complaints.

Diagnostic studies were carried out at another hospital for eighteen days, the results of which were not communicated to the patient. The patient was referred to this hospital for further work-up.

The patient was a moderate smoker, using about two cigars and six cigarettes a day for many years. For the last four weeks he had given up the use of tobacco. Past history included a removal of a pilonidal cyst in 1933, a hemorrhoidectomy in 1934, no past contact with or history of tuberculosis, no diabetes, no hypertension, and no allergies. For twenty-five years, a sinusitis had been present, treated by various means.

Physical examination revealed a middle-aged white male, somewhat dyspneic, but not appearing acutely ill. Temperature was 99.6° F. There were numerous fine crepitations and coarse moist rales present bilaterally, especially over the lower half of the chest. There was no distinct impairment of resonance or any amphoric or tubular breathing. The heart and abdomen were negative. A scaling eruption was seen on the skin of the extremities. The right inguinal and left axillary lymph nodes were tender, movable, and enlarged to bean size.

Various x-ray studies were undertaken. Reports from the other hospital were also obtained. On August 13, 1951, the liver edge was felt three finger-breadths below the costal border. There was a macular confluent erythematous rash over the small of the back and over both shoulder areas. The peripheral white blood count was 14,000 with an 18% eosinophilia, but without an anemia. Skin testing was negative for histoplasmosis, coccidiodomycosis, and tuberculosis (1:10,000 OT). After dermatologic consultation, a skin biopsy was done.

On the 5th hospital day the patient complained of back pain. There was localized tenderness over the area of T3 to T4. The skin rash had become urticarial. The patient was afebrile. Two days later information was received from another hospital that on previous hospitalization an atypical acid fast organism was isolated on bacteriological culture. These organisms were short, squat, and very red, and were not tubercle bacilli unless guinea-pig tests proved otherwise. Tests for tubercle bacilli in the Mount Sinai Hospital laboratory were consistently negative. A direct eosinophile count was 2,740. The alkaline phosphatase was 17 units.

In the next few days a three plus pitting edema of the ankles and feet appeared with localized tenderness over the lower ribs. The alkaline phosphatase continued to rise (23 to 35 units). Friction rubs and harsh rhonchi were heard over the right lower chest posteriorly. There was flatness to percussion in both lung bases, posteriorly. Cytologic studies of the sputum were negative for cancer cells. X-rays of the long bones were taken as well as a biopsy of a left axillary lymph node. A lung biopsy was ob-

LABORATORY DATA

BLOOD

COUNTS	RBC	Hb.	C.I.	WBC	Stabs	Segs	Eos	Bas	Sm. Lymphs	Monos
8/10/51	4.90	15.2 Gm 97.4%	0.99	14,000	0	62	18	1	16	3
8/14/51	Absolute eosinophile count 2,741/cu. mm. (N. 100-300/cu. mm.)									
8/16/51	5.59	16.2 Gm 103.8%	0.92	15,000	1	61	17	1	18	2
8/25/51		12.3 Gm 78.8%		16,200	9	55	4	0	30	2
	Absolute eosinophile count 632.7/cu. mm.									
9/5/51	4.36	13.2 Gm 84.6%	0.97	14,100 Majority of segs appear toxic.	4	80	1	0	12	3
9/7/51	Absolute eosinophile count o.									
9/8/51	Absolute eosinophile count 28/cu. mm.									
9/9/51	Absolute eosinophile count 16.6/cu. mm.									
9/11/51	Absolute eosinophile count 38.8/cu. mm.									
9/13/51	Absolute eosinophile count 11.7/cu. mm.									
9/15/51	4.03	12.8 Gm 82%	1.02	27,000 Majority of lymphs and segs. appear moderately toxic	10	85	0	0	5	0
	Absolute eosinophile count 22/cu. mm.									

BLOOD CHEMISTRY

	Serum Na	Serum K	Serum Chlor.	T.P.	A/G	Alb.	Glob.
8/11/51	136 mEq/L 313 mgm%	5.0 mEq/L 19.5 mgm%	96.9 mEq/L 567 mgm%	6.1	1.9	4.0	2.1
8/16/51				6.1	1.9	4.0	2.1
8/25/51				5.1	2.0	3.4	1.7
8/29 51	144 mEq/L 331 mgm%	6.6 mEq/L 27.7 mgm%	92.1 mEq/L 540 mgm%				
9/5/51	126 mEq/L 290 mgm%	5.0 mEq/L 19.5 mgm%	83.4 mEq/L 487 mgm%	Serum pH 7.32			

ADDITIONAL BLOOD CHEMISTRY

	Acid Phos.	Alk. Phos.	Amylase	Serum Total Calcium	Serum Ionized Calcium
8/14/51	3.0	17.0			
8/16/51		23.0	72	5.1 mEq/L 10.2 mgm%	2.5 mEq/L 5.0 mgm%
8/29/51		35			

SEDIMENTATION RATE

8/15/51 Uncorrected—26; Corrected 26. Hematocrit—50

PROTHROMBIN TIME

8/24/51 13 sec. Control—13 sec. % Clotting Activity—100.

URINALYSES	Color	Sp. Gr.	Reac.	Sugar	Acet.	Alb.	WBC	RBC	Blood	Casts
8/16/51	dark amber	1.023	5.0	0	0	0	0-2	0	0	0
9/11/51	amb. cldy.	1.017	5.5	0	0	tr.	1-2	0	0	0

SEROLOGICAL TESTS FOR SYPHILIS:

8/13/51 Kahn and Kline—negative

BACTERIOLOGICAL EXAMINATION:

8/13/51 Sputum: No acid fast bacilli seen on smear; culture: Diplococcus pneumoniae, alpha hem. Strep; non-hem. Staph. aureus; diphtheroids.

8/14/51 Sputum: No acid fast bacilli seen on smear; no eosinophiles seen; culture—normal flora (neisseria sp., alpha hem. Strep., non-hem. Strept., Diplococcus pneumoniae).

8/16/51 Sputum: No fungi seen on smear; culture—no fungi isolated other than a few fungi commonly found as lab. contaminants; culture neg. for acid-fast bacilli.

8/20/51 Sputum: No acid fast bacilli seen.

8/17/51 Gastric Washing: No acid fast baccilli seen on smear; culture neg. for acid-fast bacilli.

8/20/51 Stool: No protozoa, helminths, or ova were found; no micro-organisms commonly considered as pathogenic were grown.

8/27/51 Gastric Washing: No acid-fast bacilli seen on smear; culture negative for acid-fast bacilli.

8/28/51 Gastric Washing: No acid-fast bacilli seen on smear.

STOOL EXAMINATION:

8/20/51 Soft, unformed dark brown; no gross blood; trace chemical blood (hematest).

MISCELLANEOUS EXAMINATIONS:

8/16/51 24 hr. urine (960 cc.) Bence-Jones protein negative.

8/23/51 Sputum: 13% eosinophiles.

tained with a Vim-Silverman needle on August 27, 1951.

Proctoscopic examination was then performed, revealing a fungating area 16 cm. from the ano-rectal junction, but fecal material obscured visualization. This suspicion was not confirmed by later bowel x-ray studies.

The subsequent clinical course was rapidly downhill. Narcotics were given for pain, and deep x-ray therapy was applied to the chest for palliation. The patient expired on September 16, 1951.

Laboratory Data

Dr. I. Forman, Resident in Medicine: This patient came to us from another local hospital where the consultant felt certain that there was tuberculosis. He was so positive that he refused to bronchoscope this man. At the same time, we were told that, on cultures of sputum, an organism was grown that was acid-fast, presumably tubercle bacilli. In checking with the physicians and attendants, I understand that a colon x-ray was also done there but not a stomach plate. The patient was in good condition when he came here, but about 3 days later, he started going rapidly downhill. Besides the extensive excoriated rash over the extensor surfaces found on admission, he began to develop edema. Our first diagnosis on seeing this man was that of probable tuberculosis because of the data obtained from the other hospital. But upon looking at the chest x-ray, the diagnosis was soon questioned and we began to feel that it was a metastatic carcinoma or one of the fungus infections. We made several attempts to get in touch with the department of bacteriology which had grown out the acid-fast organisms and finally learned from a technician that they would not report it as a positive culture. Because of this, and inasmuch as Dr. Arendt and the x-ray department did not feel that it was tuberculosis, our impression was changed to a metastatic carcinoma, the primary site undetermined. Finally, by August 27th, as you heard, this man was going rapidly downhill and the peripheral edema had extended up to the groin. Since the total protein was not too low, we felt that this edema was due either to lymphatic obstruction or occlusion of the inferior vena cava. It is said that the liver was palpable 3 fingers below the costal margin, but we were never sure of the liver edge, for this man always held his abdomen very rigid, even under the influence of 3¼ gr. of sodium amytal. The elevated alkaline phosphatase at this time was explained as being due to metastases to the liver. Reports of elevated alkaline phosphatase in sarcoidosis have also appeared in the literature, but nothing bore out the diagnosis of sarcoidosis: the x-ray of the bones did not show any punched out areas and the node biopsy did not show sarcoidosis. The dramatic procedure of aspiration lung biopsy with a Vim-Silverman needle was executed, and Dr. Leroy gave us the diagnosis which we previously had felt strongly: a metastatic carcinoma. I tried to proctoscope the man at that time. He was quite weak by now. He could not maintain the position and was poorly prepared, but I thought I saw a lesion about 1 cm. above the proctoscope. It was impossible to biopsy it — the proctoscope was immediately filled with fecal material. We could not attempt to reproctoscope him because of his condition, which was rapidly downhill. Dr. Leroy felt sure that the lung biopsy slide demonstrated the metastatic lesion as being from some place in the gastro-intestinal tract.

Dr. N. I. Fox, Internist: I did not see this patient. From what is recorded here there was an enlarged liver. Whether that was a primary carcinoma of the liver or a secondary carcinoma remains to be seen. He was an alcoholic, or might have been an alcoholic, being a liquor salesman. The question of a primary carcinoma in the liver with metastases to the lungs has to be considered. The enlarged liver is one of the things that gives us a lead as to a possible primary malignancy. Another matter is the crater-like ulceration of the rectum about 16 cm. above the anal opening found by Dr. Forman on proctoscopy. It could have been a malignancy which had metastasized to the liver and to the lungs. Whether he could have also had a pros-

tatic malignancy with metastases to the lungs, is something we have to consider, although he was rather young. On the whole, it is anybody's guess where the primary malignancy was and the pathologist, as usual, will have the final say.

Dr. I. A. Rabens, Internist: I saw this man the day after his admission. At that time, with the findings in the chest and with the story of expectoration of cupfuls of sputum, we felt that he might have had a good deal of bronchiectasis with diffuse bronchitis. But when we saw the x-ray picture, it looked more like a bronchogenic spread of an aspiration tuberculosis, especially when we heard there was a report from another hospital that they had found something that looked like tubercle bacilli, although none were subsequently found here. The differential diagnosis, on that day, was between a bronchogenic spread of tuberculosis or a carcinomatosis of the lungs. We favored more a carcinomatosis at the beginning. The proctoscopy showed a suspicious lesion which was not visualized on x-ray studies in this hospital. The biopsy of the lung, of course, made the diagnosis later.

Dr. D. Cohen, Dermatologist: When we saw this man at dermatologic consultation, he looked in fairly good shape and, of course, his outstanding complaint was his cough. His skin eruption was not sharply defined. One couldn't make an accurate diagnosis from his skin alone, but because of the chest condition and the eosinophilia, we thought of some member of the lymphoblastoma group as a possibility. He had a lot of pleuritis and eosinophilia. The rash was urticarial in some spots, macular and papular in others. We suggested a biopsy, but it didn't show anything specific. Of course, in this great group of lymphoblastomas, one more often sees a so-called allergic rash rather than a true infiltrate. However, the biopsy did not show any true infiltrate. We then toyed with the interesting possibility of a cutaneous manifestation of a pulmonary fungus disease, which we are always looking for; but it is hard to prove a dermatitis due to a fungus unless we can isolate the fungus from the pulmonary secretions. This was all done before the gland was taken for histological examination, which, of course, put us at a little disadvantage. His treatment was merely symptomatic.

Dr. H. Kamin, Cardiologist: This patient had an electrocardiogram taken which did not contribute much. Essentially, it was a normal electrocardiogram, with an isoelectric S-T segment, regular and upright T waves and a normal AVL. The second ECG tracings were essentially normal, too.

Dr. J. Arendt, Roentgenologist: The introduction gave us a clinical diagnosis of tuberculosis of the lungs and the information that at least one sputum had been found positive for tuberculosis. Our x-ray film showed a snowstorm of densities extending over both lungs, some fluffy and some round, filling the entire depth of the lung, and therefore superimposed and confluent. In certain places, where the densities were farther apart, we could make out the basic pattern of nodularities and reticulations. We also found the hilar glands enlarged. Our conclusion was that the picture was more consistent with malignancy than tuberculosis.

The second problem which arose in the absence of any leading symptom was whether we were dealing with a primary or a metastatic malignancy. Among the primary tumors of the lung which might give such a picture, is notably the rare condition known as pulmonary adenomatosis or "alveolar carcinoma." A complete work-up was suggested. We found no evidence of metastasis in those bones which came under observation.

The stomach, as seen in our films, showed a distinctly normal outline, normal mucosal pattern, and normal emptying. The small bowel had a normal appearance.

The examination of the colon demonstrated a good filling. The flexures of the sigmoid were very carefully examined and no defect was noted either in the mucosal pattern, in the complete filling, or in the air insufflation. The mucosal filling showed an uninterrupted regular pattern, ruling out any malignancy down to the rectum. The examination

of the rectum, however, is the domain of the proctoscopist and digital examination should always precede roentgenological examination. The ampulla recti, when filled with barium, is a pouch of considerable distensibility wherein a protruding, non-contracting, malignancy might be completely hidden. It is well known, and has been frequently pointed out in all text books, that roentgenologists should accept the responsibility for the detection of malignancy from the sigmoid upward, and that the rectum itself, however, should be directly examined and digitally explored. It was possible in this case to see the lesion directly, as Dr. Forman told us, but unfortunately it was rather late, the patient was going downhill and the lungs were studded with densities, so that the discovery of the primary lesion was of little practical value.

To have a clean bowel without fecal material is as important to the radiologist as it is to the proctoscopist. Fecal material is a soft mass which protrudes into the lumen. A filling defect caused by a polyp or by a fecal ball would have the same appearance. Preparation is the first condition for a successful colon examination.

Postmortem Examination

Dr. I. Davidsohn, Pathologist: The organs of interest included the lungs, which together weighed 3,200 Gm. (N. 792 Gm). They were voluminous and extremely firm in consistency (Fig. 1). The outer surface (Fig. 2) was streaked with numerous confluent bands of grayish white material within dilated lymphatics and blood vessels; the background was a deep reddish gray. The sectioned surface was a variegated mixture of tangled infiltrating grayish white tumor tissue. None of the bronchi on the mucosal aspect showed any tumor. The involvement of the lungs was that of metastatic carcinoma.

There were also numerous metastases in the mediastinal, periaortic, peripancreatic, mesenteric, and retroperitoneal abdominal lymph nodes.

The primary tumor was in the rectum, located about 11 cm. above the anus (Fig. 3). The tumor was bulky, very soft, ulcerated on the surface, and occupied about one-half of the circumference of the bowel. In one area was seen a constriction ring with some puckering of the mucosa, involving the wall also. Proximal to this site there was only slight dilatation. In other words, there was no distinct obstruction of the lumen of the bowel in normal function.

Microscopic sections of the tumor revealed well-preserved carcinomatous glands with some irregularity of structure and appearance. In some areas, carcinoma was present only in the submucosa and the mucosa was still fairly normal in appearance. A nearby lymph node revealed metastatic infiltration by carcinoma.

We are thus dealing with a carcinoma of the rectum about 11 cm. above the anus, not very large, apparently not interfering with the normal function of the bowel, as evidenced by the fact that the dilation of the proximal portion of the bowel, if present at all, was only moderate. Certainly there was no hypertrophy of the wall. There were metastases to all the lymph nodes — regional, mesenteric, periaortic, peripancreatic—and metastases to the liver, lungs, and bones.

Anatomic Diagnoses

Infiltrating, ulcerative adenocarcinoma of the rectum with metastases to the lungs (carcinomatous lymphangitis and carcinomatous pneumonia), to various lymph nodes, liver, peritoneum, pleura, pericardium, bone (second lumbar vertebra and ribs), and cerebellum (right lateral lobe). Bilateral hydrothorax. Chronic bronchopneumonia. Acute and chronic passive congestion of the spleen. Edema of the lower extremities. Hydrocele of the right testicle (tunica vaginalis).

Cause of Death:

Carcinoma of the rectum with widespread metatases.

Summary and Discussion

Dr. Davidsohn: The reason this case is of interest is that it presented considerable diagnostic difficulties. The cancer did not produce local obstructive changes at all. In addition, one would like to

have the answer to the following question: why did this carcinoma produce such extensive metatases?

The question that interests the surgeon at operation is what prognosis he should make in a case of carcinoma of the bowel.

Dukes, of St. Mark's Hospital in London, has done more work on the pathology of carcinoma of the colon for the past 28 years than anyone else. That hospital is devoted exclusively to rectal and colonic work, and we owe a great deal of our knowledge about these tumors to Dukes. According to his classification, which I shall follow, this tumor is one which grows into the lumen of the bowel, a carcinoma protuberans, which has, as a rule, a fairly good prognosis. However, the present case did not comply with the rule, as is so frequently the case with cancer.

Dukes divides these carcinomas into protuberant, ulcerative, fibrosing or scirrhous, and so-called malignant adenomas and malignant papillomas. Inasmuch as papillomatous adenomas of the large bowel are definitely premalignant, they should be included in this classification. This is the classification on the basis of gross findings.

According to microscopic features, carcinoma of the colon is classified by Dukes into adenocarcinoma, which constitutes about 80 to 90% of all carcinoma of the colon, mucoid carcinoma, and finally, anaplastic carcinoma or carcinoma simplex. According to this classification the lesion in this case would be an adenocarcinoma.

Finally, a significant contribution by Dukes is his conclusion that the prognostic criteria based on this gross and microscopic classification are not reliable, although it is true that, in adenocarcinomas, the degree of malignancy is frequently dependent upon the maturity of the cells. He thinks that the most important thing is to evaluate the spread of the tumor at the time of operation. In other words, a carcinoma which involves only the wall of the bowel, including the muscularis, is graded as Class A. If it infiltrates deeper and involves the serosa also, it is graded as Class B. When it involves the lymph nodes in the mesentery, it is in Class C. If a visceral organ is involved by metastases, the class is D. The prognosis depends also upon another criterion, which seems to have as much significance, or even more, than involvement of the lymph nodes, namely, the presence of tumor masses within the lumens of blood vessels of the wall of the bowel. This has been the subject of considerable investigation recently and its presence makes the prognosis particularly bad. I think that the presence of this form of involvement, namely entrance of the tumor into a vein, is the determinant factor in the spread of the tumor. That was what this case showed (Fig. 4). In other words, it isn't so much the size of the tumor, or the degree of obstruction that is produced, or even the microscopic appearance, which is most important but it is the involvement of the lymph nodes, which may be seen grossly, and invasion of the veins, which can also be seen grossly, especially if larger veins are invaded.

The so-called fibrosing carcinoma, which is frequently considered as being highly malignant, frequently does not live up to that bad reputation because of its early manifestation due to stenosis. Because of this it is recognized and operated early.

Dr. I. A. Rabens: What is your opinion about the report of a positive culture of an acid-fast bacillus isolated from the sputum at the other hospital?

Dr. Davidsohn: It apparently was not recognized as a tubercle bacillus because it did not produce the characteristic lesion when injected into guinea pigs. We shall call on the bacteriologist to tell us more about that.

Dr. H. Isaacs, Internist: Were the adrenals involved?

Dr. Davidsohn: The periadrenal fat was involved; but the adrenals proper were not.

Dr. L. Edidin, Internist: How do you account for the eosinophilia?

Dr. Davidsohn: The patient had a chronic dermatitis. We had a biopsy of the skin and found nothing but a chronic dermatitis. What it was, I don't know. Occasionally, eosinophilia has been re-

ported in extensive carcinomatosis. It may be that the necrosis which accompanies the process is responsible for the eosinophilia.

Physician: How old would you say this lesion of the bowel was?

Dr. Davidsohn: It was an ulcerative carcinoma. I don't think that I can say how old it was. From the extension of the lesion, it probably could be stated that it was a few months old, to say the least. The widespread tumor is compatible with the small primary lesion. The lesion doesn't have to be very large because, once the veins are invaded, the spread all over the body doesn't take very long.

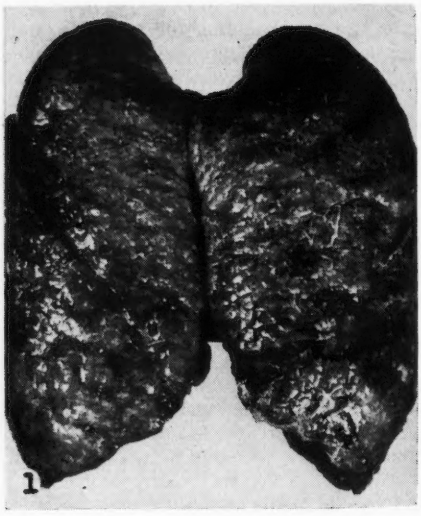
Physician: Were the lesions of the lungs quite old in view of the long-standing pulmonary symptoms?

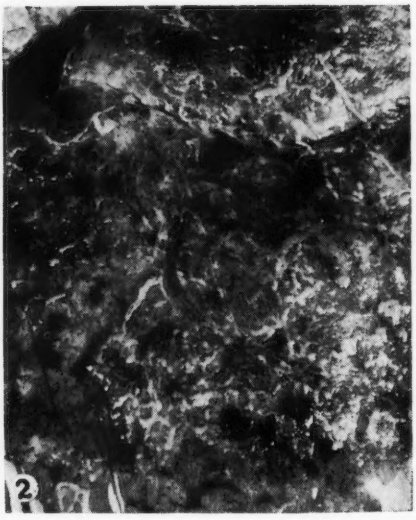
Dr. Davidsohn: I believe that the symptoms referable to the lungs can be very well explained by the chronic bronchitis and chronic bronchopneumonia and that the carcinomatous spread was hardly, if at all, responsible for them.

Mr. Goldin, Bacteriologist: Just a few words about the non-pathogenic acid-fast bacilli. It must be realized that many organisms are acid-fast and closely related to the tubercle bacillus, but they are not virulent. We are all familiar with the smegma bacillus, the timothy bacillus and so on. They are quite common, especially nowadays, in secretions from a patient who has been exposed to antibiotics. We find them more and more frequently because these organisms are invariably resistant to penicillin, aureomycin, *etc.*, the same as the tubercle bacillus. Consequently, unless the acid-fast bacilli have the cultural characteristics and invasiveness of a tubercle bacillus, these organisms have no more significance than a saprophytic organism, and the reports of the laboratory must be interpreted with caution. These organisms are particularly found in gastric washings, and acid-fast bacilli found directly in a gastric washing does not mean that they are necessarily tubercle bacilli. Only by the typical colony morphology on special media and by animal virulence studies can you prove that they are tubercle bacilli. So, one must be quite cautious about the interpretation of the presence of acid-fast bacilli.

BIBLIOGRAPHY:

1. Dukes, C. E.: Cancer of the Rectum, an analysis of 1000 cases. J. Path. & Bact. 50:526-539 (1940).
2. Dukes, C. E.: The Surgical Pathology of Rectal Cancer. Pros. Roy. Soc. Med. 37:131-144 (1944); 38:381 (1945).





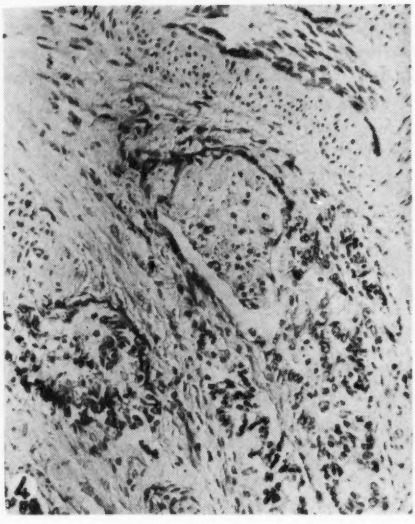


Fig. 1. Enormously enlarged and voluminous lungs, weighing 3200 gm. (N. 792 gm.) and invaded by metastatic carcinoma. The consistency of these lungs was quite firm.

Fig. 2. This closeup of the pleural aspect of the lungs demonstrates the surface streaks of carcinoma within dilated lymphatics and blood vessels. This is called carcinomatous lymphangitis.

Fig. 3 The primary tumor of the rectum at 11 cm. above the ano-rectal junction. This relatively inconspicuous lesion was the source of this patient's widespread metastases.

Fig. 4. Rectum: tumor thrombus in lumen of a blood vessel. This phenomenon is regarded as the determinant factor in the spread of the tumor. Photomicrograph X150.

BOOK REVIEWS

A TEXTBOOK OF CLINICAL NEUROLOGY. By Israel S. Wechsler, M.D. Cloth. 801 pages with 179 illustrations. Seventh edition. Philadelphia: W. B. Saunders Company, 1952. $9.50.

In this book, Dr. Wechsler has kept pace with the recent advances in the field of neurology and has extensively revised the previous edition to accomplish this. The treatment of the meningitides, especially tuberculous meningitis as well as other infections of the nervous system has been completely revised. The treatment of neurosyphilis has been thoroughly modernized. The classification of the encephalitides has been brought up to date and cerebral aneurysms and angiography have received critical attention. In addition chapters on management of injuries of the brain and spinal cord and the surgery of tumors have been improved to accord with newer knowledge. The Meniere syndrome has been brought up to date, cerebellar function has been reconsidered and electromyography and double simultaneous stimulation are newly incorporated. A number of new illustrations have been introduced and many old references deleted to make room for the new ones. This book, although not quite comprehensive enough for a standard reference text is excellent as a standard textbook for senior medical students and as a reference text for the general practitioner.

BIOCHEMISTRY FOR MEDICAL STUDENTS by William Veale Thorpe, M.A., Ph.D. Cloth. Fifth edition. 528 pages with 41 illustrations. J. P. Lippincott Company; Philadelphia, London and Montreal. 1952. $6.00.

The fifth edition of this text contains revisions of the chapters on metabolism, detoxication, enzymes, proteins, hormones and vitamins. Attention has been given to the newer knowledge derived from isotope studies. Generally, the organization of the book is unchanged. The bibliography should be expanded in future editions. It is recommended as a basic science text for medical students.

SURGERY AND THE ENDOCRINE SYSTEM by J. D. Hardy, M.D., F.A.C.S. Cloth. First edition. 153 pages with 43 illustrations. W. B. Saunders Company, Philadelphia and London. 1952. $5.00.

The approach to pre- and post-operative care of surgical patients has been modified greatly in the light of newer advances in the field of endocrinology. The author has presented in a most lucid manner a resume of current knowledge of the physiology of surgical trauma and the principles of treatment proceeding therefrom. Physiologic considerations and principles of surgery of the endocrine glands themselves are excellently summarized. In addition to numerous informative illustrations and figures, the book contains concise charts which highlight the subjects under discussion. The bibliographies are current and extensive. The material, which is both complex and controversial, is handled in a simple, practical fashion and gives both general practitioners and surgeons a valuable guide to "hang their hats on".

INTRODUCTION TO MEDICAL SCIENCE by Julius Jensen, Ph.D. and Henry Noller, M.D. Cloth. First Edition. 533 pages with 65 figures. St. Louis: The C. V. Mosby Company, 1952. $5.75.

This book, evidently written for an introductory course in nursing, has as its purpose, a general coverage of the entire field of medicine. Despite the fact that a definite scientific background is required for the comprehension of the more technical material, the presentation is very superficial. Although almost totally inadequate from the medical student and practitioner's viewpoint, this book can be used as a survey of medicine for nursing and medical technician students.

HISTOPATHOLOGICAL TECHNIC by A. A. Krajian, Sc.D. and R. B. H. Gradwohl, M.D. Cloth. Second edition. 362 pages with 131 illustrations and 7 color plates. The C. V. Mosby Company, St. Louis. 1952. $6.75.

This manual of technic is designed primarily for technicians, research workers and laboratory directors. Histochemistry has undergone much advancement in recent years and the book has been thoroughly revised to include most of the current methods. Some of these include serumizing, Autotechnicon methods, reticulum, elastic, amyloid, and myelin sheath stains and Papanicolaou procedure. Brief discussions of principles involved and sources of error amplify the material on procedure. The book is an excellent reference manual for research and laboratory workers.

BRONCHOESOPHAGOLOGY by Chevalier Jackson, M.D., Sc.D., LL.D., F.A.C.S. and Chevalier L. Jackson, M.D., M.Sc., F.A.C.A. Cloth. First edition, reprinted. 366 pages with 260 figures including color plates. W. B. Saunders Company, Philadelphia and London. 1950. $13.00.

This book represents a compilation of material previously presented in the illustrious authors' classic textbook on bronchoscopy and esophagoscopy, to which have been added chapters on diseases and abnormalities of the tracheo-bronchial tree and esophagus. The science of bronchoesophagology is a comparatively new addition to the medical sciences. This book presents a functional and anatomic approach to the subject for the benefit of bronchoesophagologists. Endoscopy has assumed great importance in the diagnosis of various conditions of the organs in question. The technics of bronchoscopy and esophagoscopy as practiced so successfully for many years by the authors are clearly and succinctly explained and elaborated. Excellent diagrams and illustrations abound throughout and serve to make this a monumental exposition. The appendix contains a thorough description of all instruments employed. The bibliography is exhaustive. This book is too advanced for the medical student and practitioner, but is invaluable for the specialists in the field and anesthesiologists.

ABSTRACTS SECTION

KOENIG, H. and STAHLECKER, H.: Cytoplasmic protein in normal neurones and its morphologic and quantitative alterations in the axone reaction. The Anatomical Record, V. 109, No. 2, Feb. 1951.

The nucleoprotein nature of the Nissl body was demonstrated by Landstrom, Caspersson, and Wohlfart (1951). Hyden (1943) and Gersh and Bodian (1943) employing Caspersson's method, have studied quantitative changes in nucleic acid and protein in the axone reaction. Because their protein data is open to criticism and their studies provide little morphological information, this study was undertaken.

The Millon reaction was employed on cat spinal cord in which one sciatic nerve had been cut at varying times prior to sacrifice. Quantitative determinations of light absorption at 476 mμ were made with a photometric technique and expressed as extinction coefficients. The cytoplasm or normal neurone is uniformly colored except for areas resembling Nissl bodies which are colored more intensely. Nuclear membrane and nucleolus give intense reactions. This reaction is prevented by peptic digestion but uninfluenced by extraction of ribosenucleic acid with 10% perchloric acid.

Nerve cells undergoing the axone reaction show disruption and solution of the protein matrix of the Nissl bodies which closely resemble and parallel classical chromatolytic changes. These alterations are seen also in sections stained with the acid fast-green dyes and eosin, and the Sakaguchi test for arginine (basic proteins). Quantitative studies are in progress. Six days after nerve section neurones show a reduction in cytoplasmic protein of 7.3%, at 14 days, 32.2% and at 41 days, 17.8%.

KOPPER, PAUL H. Relationship of Growth-Phase to the Reducing Activity of Bacterial Cells, Nature, *167*, 951 (1951).

Pretreatment of 18-hour old *E. coli* cells with veal infusion broth and without sodium nitrate induced an increase in the yield of sodium nitrite, when the washed bacteria subsequently were allowed to act on sodium nitrate. Young cells of the same organism, grown for 3, 4 and 5 hours, were far more active than 18-hour old cells in reducing sodium nitrate and methylene blue. These findings indicate a direct relationship of the synthetic, energy-requiring processes of the lag and log phases of bacterial growth to high reducing activity.

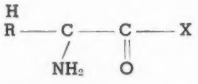
GOLDFARB, A. R. and SAIDEL, L. J. Ultraviolet Absorption Spectra of Proteins. Science *114*:156-7 (1951).

An absorption band for proteins and peptides is described with a maximum at about 1950 A. Data collected for the extinction coefficient at 2050 A has been used that each peptide band contributes about 2800 to the molar extinction of the protein. A preliminary report.

SAIDEL, LEO J.: The Ammonia Evolved from Peptides and Proteins by Ninhydrin (presented at the National Meeting of the American Chemical Society in Chicago, September 5, 1950).

Most amino acids react with ninhydrin at 100°C at pH 2.5 to yield one mole of ammonia per mole of amino acid. Of a number of glycyl, alanyl, leucyl, and phenylalanyl peptides, amides and esters only glycyl peptides and esters yielded close to one mole of ammonia per mole of reactant under the above conditions. The other amino acid peptides, amides, and esters yielded only 0.02 to 0.06 mole. Glutamine and glutathione yielded close to one mole.

The data indicated that if X═OH in the compound below, the compound would yield ammonia when treated as above, independently of the nature of R, but that if X═NH_2, NHR', or O-R", then the compound would yield ammonia only when R═H.



The slight ammonia evolution by proteins under these conditions was discussed in relation to their terminal glycyl content.

CLARK, GEORGE, GOLDZBAND, M. G., and GOLDBERG, S. E. Cessation of Walking Elicited by Stimulation of the Forebrain of the Unanesthetized Dog. Amer. J. Physiol. *167*:127-133, 1951.

Electrodes were implanted aseptically at various subcortical locations in a series of dogs, and the animals were tested on the day following operation when they were awake and alert. Stimulation (60 cycle sine wave) at most of these points produced a cessation of spontaneous walking with no apparent loss of postural tone. Often there was some movement, such as turning the head, associated with this arrest. Supraliminal stimulation elicited various complicated clonic movements outlasting the stimulus. These were often so intense and generalized as to be best described as convulsions. The active points were widely scattered in the white matter and included internal capsule, corona radiata, fornix, corpus callosum, etc. Several were located near the border of the caudate nucleus but arrest was not elicited from points centrally located in the caudate nucleus. A similar (?) cessation of spontaneous walking in the cat was termed "supression" by Ward and the "arrest reaction" by Hunter and Jasper. It is difficult to see how either of these terms can be applied to the response we have observed.

SCHOOL NOTES AND NEWS

The entire student body, Faculty, and Alumni extend their heartfelt sympathy to the family and friends of Dr. David A. Willis, who died May 20, 1952 at the age of 52.

With the untimely passing of Dr. Willis, Associate Professor of Surgery, The Chicago Medical School has lost one of its most beloved faculty members. Since his appointment to the staff in October 1947 Dr. Willis has devoted himself to his students and has in this short period of time come to be admired by all those who knew him.

Dr. Willis received his undergraduate and medical training at the University of Illinois, being granted the degree of Doctor of Medicine in 1922. Additional postgraduate studies in Pathology were carried on at the University of Illinois. Following internship at Cook County Hospital, Dr. Willis maintained his practice in Chicago, ultimately holding the post of Attending Surgeon at Mount Sinai Hospital.

Dr. Willis was a Diplomate of the American Board of Surgery and a Fellow of the American College of Surgeons. Other organizations in which Dr. Willis actively participated include the American Medical Association, the Chicago Medical Society, and Sigma XI.

The late Dr. Willis also carried on numerous research projects and found time to contribute publications to many journals. Recognition for his interest in medical students and their education was manifested by the World Health Organization of the United Nations when they granted him a Fellowship for the purpose of observing medical education methods in European countries. This study was carried on from September through November, 1950.

Dr. Willis will always be remembered as a source of inspiration and guidance to the many students who had the privilege of working with him.

FACULTY NEWS

It is with great pride that we take this opportunity to welcome Mr. Milton Geerdes to the Administrative Staff of The Chicago Medical School. To the position of Registrar Mr. Geerdes brings a great deal of specialized training which will be of extreme value in the fulfillment of his recently acquired duties.

A Chicagoan by birth, Mr. Geerdes followed his secondary education in Chicago schools with studies at Calvin College, Grand Rapids, Michigan, leading to the degree of Bachelor of Arts. After this our new Registrar continued his schooling at George Williams College in Chicago, pursuing a course for which he was granted, in June, 1949, the degree of Master of Science in Education. The granting of this degree was followed by enrollment at The University of Chicago, where Mr. Geerdes is now in the process of completing his studies for the title of Doctor of Philosophy in Student Guidance.

Mr. Geerdes has been active in community affairs, being especially interested in YMCA activities, having served as a Director of a YMCA Day Camp in Chicago, as well as Program Director of the "Y" College Camp in Lake Geneva, Wisconsin. Other activities of administrative capacity were experienced by Mr. Geerdes during his four-year term of service in the United States Navy. While in the Pacific Theater of Operations, Lieutenant Geerdes was a Communications and Executive Officer.

We take great pleasure in welcoming Mr. Geerdes to The Chicago Medical School and trust that his association with us will be a long and beneficial one.

Fourteen members of the faculty, including President John J. Sheinin, appeared on the program of a conference in Dixon, Illinois, on Thursday, April 17. This conference was arranged by the Postgraduate Education Committee of the Illinois State Medical Society in cooperation with The Chicago Medical School. During the course of the conference Dr. Sheinin spoke on "Medical Education for General Practice."

Department of Anatomy

Assistant Professor Hans Elias has received a grant of $4,320 from the National Heart Institute of Bethesda, Maryland, for "Study of the Three Dimensional Structure of the Human Adrenal Cortex in Normal and Hypertensive Persons."

Department of Anesthesiology

Heartiest congratulations to Dr. and Mrs. Bernard K. Galston (Associate in Anesthesiology) on the birth of Judith Iris' brother, Steven G., on April 25, 1952.

Department of Biochemistry

Congratulations to Dr. and Mrs. Leo J. Saidel on the birth of a son, Matthew Louis, on February 13, 1952.

Department of Medicine

Dr. Herman L. Eisenberg was elected to associate membership in the American College of Physicians at their recent convention at Cleveland, Ohio.

Dr. Aldo A. Luisada has been elected to membership in the Chicago Society of Medicine and the Illinois State Medical Society.

Department of Neurology and Psychiatry

Congratulations to Drs. Judith and LeRoy Levitt on the birth of a son, Steven, on April 17, 1952.

Department of Ophthalmology

Dr. Samuel I. Kauffman has been appointed Attending Ophthalmologist at Mount Sinai Hospital.

Department of Pediatrics

Congratulations to Dr. and Mrs. Gordon Cherwitz on the birth of a son, Richard Arnold, on January 11, 1952.

Department of Physiology

Congratulations to Dr. and Mrs. Ben B. Blivaiss on the birth of a son, Mitchell Sherwin, on March 2, 1952.

STUDENT NEWS

Both the Freshman and Sophomore classes held elections recently and chose their officers for the coming year. Elected to office in the class of 1955 are:

Edward Altchek, President; Marvin Herz, Vice-President; Alicia Barach, Secretary; Jeanette Chang, Treasurer; and Stuart Eichenfield and Morton Lacher, Student Council Representatives.

Results of the elections of the class of 1954 are as follows:

Theodore Feldman, President; James Keuer and Melvin Samuels, Vice-Presidents; Robert Cerfolio, Secretary-Treasurer; Stanley Bauer, Student Council Representative (two-year term); and Saul Zimmerman, Student Council Representative (one-year term).

Class of 1952

Best wishes to Lester Schwartz on his engagement to Miss Grace Silverstein of Chicago, Illinois.

We wish to congratulate Mr. and Mrs. Edward Weissman on the birth of their son, Keith, on March 2, 1952.

Even before graduation, George Ehrlich and Melvin Levinson have brought honor to themselves and their Alma Mater by receiving the second prize in the 1952 essay contest sponsored by *The New England Journal of Medicine*.

It has been announced in a recent issue of *The Diplomate* of the National Board of Medical Examiners that Robert Tan-Beth, on April 16, 1952.
nenbaum achieved the highest grade in Biochemistry on the National Board Examination (Part I) given in January.

Class of 1953

Best wishes to Mr. and Mrs. Donald Behr on the birth of their son, Bruce Martin, on January 12, 1952.

Congratulations to Marvin DeHaan on his marriage to the former Miss Marilyn Johnson of Detroit, Michigan, on March 22, 1952.

We offer congratulations to Gerald Weiner on his marriage to the former Miss Naomi Jacobson of Chicago, Illinois, on March 16, 1952.

Class of 1955

We wish to congratulate Maury Fields on his marriage to the former Miss Nina Shepard of Brooklyn, N. Y., on March 23,

ALUMNI NEWS

Class of 1934

Dr. L. J. Jurek has recently been appointed representative from the Illinois State Medical Society to the Advisory Committee for The Chicago Medical School chapter of the Student American Medical Association.

Class of 1939

Lieutenant Colonel Samuel G. Perry is at present stationed in San Francisco, California.

Class of 1942

Dr. Julius Brant is now a Captain in the United States Army Medical Corps and is stationed at the United States Infirmary, Black Hills Ordnance Depot, South Dakota.

Congratulations to Dr. and Mrs. Samuel J. Cohen on the birth of their daughter, Carol Maxine, on February 26, 1952.

Class of 1944

Captain Herbert Smulson of the United States Army reports that he is now stationed in Chunchon, Korea, following service in Hawaii, Wake Island, and Japan.

Class of 1946

The marriage of Dr. Eugene J. Rogers to the former Miss Joyce Lighter of Seattle, Washington, took place on February 9, 1952.

Class of 1947

Dr. Muriel E. Griffith has been granted a license to practice in the State of Alabama.

Dr. Leslie S. Lowenthal is now stationed in Korea and has recently been promoted to the rank of Captain in the United States Army Medical Corps.

Dr. Albert B. Chatzinoff is now serving as a First Lieutenant in the United States Army Medical Corps.

Class of 1949

Dr. Hyman I. Kaplan has announced the opening of his new office at 2422 E. 75th Street, Chicago, Illinois.

Dr. Bernard Kleppel, President of the Class of 1949, has received a Fellowship in the Department of Radiology of the University of Minnesota Hospitals, service to begin in July, 1952.

ORGANIZATION NEWS

Student Council

When the student council was formed in the fall of 1949 its purpose was stated in its Preamble:

To coordinate student activities.

To create closer relationships between the students, faculty, administration and student organizations.

To aid all fellow students.

To obtain student cooperation in maintaining the high educational standards of the school.

To enhance the reputation of our medical school and its graduates.

In summarizing what has been done, it is important to realize that the Student Council played only part of a role in these accomplishments. Without the cooperation of the entire administration and students, many advances could not have been accomplished. Therefore we wish to thank everyone who has contributed toward the goals which we have tried to attain.

What has then been achieved?

The Maurice Oppenheim Memorial loan fund.

Half of the dues which students pay to the Student Council goes towards this fund. Graduation class gifts to the school have aided materially in raising the amount of money available.

Any student who desires a loan may receive one without question and without interest. Due to the small amount of money available only loans up to $75.00 are at present available, but whatever is available is there at any time. The integrity of each student is ample protection that the loan will be repaid. We hope that in the near future some benevolent graduate or friend will contribute toward making this fund even more useful.

Freshman Program.

Each fall as the new class enters CMS all upper-classmen remember how they felt when they entered school. For the last two years the Council has held a Freshman Meeting. We meet with the

Freshmen, try to find them housing and tell them something about Chicago and the opportunities at The Chicago Medical School. The President of each student organization is presented to the Freshmen to describe the function of the individual organizations. We introduce them to student activities, and hope we can make their introduction to medicine a better adjusted and happier one.

Internship Information.

In the library may be found answers to questionnaires which the Council was permitted to send to interns graduated from CMS. These questionnaires may be of value in helping seniors decide on their choice of an internship.

Student Directory

This year, the long delayed directory became a reality. It is not the biggest, best, or prettiest edition of its kind, but it is a start.

Identification cards.

This year, for the first time, students at CMS have been given ID cards. These cards, in establishing identity, have proved to be of value in many ways.

Student Key.

We now have available for graduating members of CMS a school key. We hope that each student will take advantage of the privilege of wearing the CMS key when he leaves as a graduating senior.

The Foramen.

This little publication, erratic at times we admit, is published with the hope that our students will have a means of knowing what the Council is doing. It will also serve as a sounding board to get your comments.

School Dance.

On April 19 of this year the first annual spring dance sponsored by the Student Council was held at the Hamilton Hotel. A large proportion of the student body was in attendance and, as you already know, a good time was had by all. It is hoped that this annual dance will prove to be the social highlight of the year for the whole student body.

There are many other things, small in their way, which we have done to make CMS a better place. Bear in mind that everything we as students feel we want or need may not always be in our own best interests or in the best interests of the school. In trying to do better things we must seek higher and wiser counsel for advice and information.

We in the Council are trying to build something intangible. We want school spirit to continue to be a real thing and we earnestly hope that every member of the student body will do his part. Your cooperation, your help, your criticisms, your ideas are all necessary and welcome. Together we can enhance the pride we feel in our school.

Stuart Cohn, President,
Student Council

* * * *

Late in the Spring Quarter elections were held by the Student Council for Officers for the 1952-53 school year. The results are as follows:

President ..... Robert Langs
Vice-President ..... Fred Cohen
Secretary ..... Stanley Bauer
Treasurer ....Donald Behr

Phi Lambda Kappa

Another year packed with activities for the Alpha Rho chapter of Phi Lambda Kappa has now drawn to a close. Due to the untiring efforts of the Education Committee, Phi Lambda Kappa has been able to present to the entire student body another excellent series of lectures intended to integrate our studies with all spheres of medicine, socio-economic as well as clinical. The closing lecture was given April 8, 1952, by Mr. Richard Netzer, of the Department of Internal Revenue. His enlightening speech was on the topic "Socio-Economic Aspects of Medicine," and was very well received by the members and their guests.

On May 8, 1952, the annual Dinner-Election meeting was held. Balloting resulted in the election of the following group of officers for the school year 1952-53: Kenneth Cohen, President; Eugene

Trachtenberg, Vice-President; Jerome Gold, Secretary; Donald Behr, Treasurer; Irwin Krasna, Corresponding Secretary; Larry Shuman, Alumni Scribe; and Sander Breiner and Sheldon Waldman, Student Council Representatives.

We were very privileged to have present at the meeting one of our recently appointed Faculty Advisors, Dr. LeRoy P. Levitt. Dr. Levitt presented a lecture on "Physician-Patient Relationships," with emphasis on the phase concerning patients with psychosexual conflicts.

On May 24, 1952, we enjoyed the highlight of the social year for Phi Lambda Kappas of Chicago. The annual Senior Dinner Dance, looked forward to by alumni as well as fraters of The Chicago Medical School and University of Illinois chapters, was held at the Furniture Club. On this occasion the Alpha Rho chapter of Phi Lambda Kappa presented the first Annual Gold Medal Award to President John J. Sheinin as "the individual associated with the school who has done the most for the student body." This is, to our knowledge, the first award of its kind to be presented in the history of The Chicago Medical School. Home talent, headed by Hub Segal, Ted Feldman, and Ken Cohen provided the entertainment for the affair, in a show never to be forgotten by all of our members and guests.

Highlighting a number of innovations in the chapter's activities this year was the introduction of *The PLK News.* Planned by Editor-in-Chief Jerry Rosenberg, this publication has already shown many indications of a very promising future. This official chapter newspaper serves primarily as a means of keeping all of our fraters and alumni informed as to current and future activities.

Phi Delta Epsilon

With the end of the spring quarter, Beta Tau Chapter will have wound up an extremely eventful year. The chapter was enriched by the addition of a record number of initiates who promise to maintain the high standards set by the fraternity in the educational and social world of CMS. Our graduating seniors carry with them our every wish for their continued success.

Speaking of graduating seniors, we wish to congratulate Joe Roche for his supreme scholastic standing in his class, and also George Ehrlich, for his appointment as the chapter's "Outstanding Undergraduate of the Year." These men, along with their confreres in the senior class, were feted at a dinner dance held at the Tam O'Shanter Country Club late in May. Many of the Phi Dee E faculty members joined the chapter in celebration on that date.

With the coming of summer, the activities of the chapter will be held on an informal basis, but when the fall quarter rolls around the fraters will again begin the cycle of fraternity events which are expected to be augmented under the able leadership of our Consul, Jack Handel. Other officers for the coming year are Vice Consul, Sherman Goldberg; Scribe, Norman Shapiro; Marshal, Eugene Shatkin; Chancellor, Marvin Levenson; Assistant Chancellor, Jason Greenstein; Historian, Melvin Goldzband; Senior Senator, Clayton Jones; Junior Senator, Fred Cohn; and Graduate Senior, George Ehrlich. However, at the moment we wish our new junior class a happy vacation and send our usual "Don't work too hard" to the sophs and seniors.

Association of Interns and Medical Students

At a meeting late in the winter quarter the following members of the chapter were elected to serve as the officers for the year beginning in the spring quarter, 1952: Sanford Lazar, President; Joseph Malerstein, Sophomore Secretary; Maury Fields, Freshman Secretary; and Bill Kalt, Treasurer.

Student American Medical Association

The SAMA-sponsored lecture on March 5 by Dr. Philip Thorek was attended by an overflowing audience. His subject was "The Acute Abdomen." This was followed on April 23 by an informative talk by Dr. Rachmiel Levine on "The Pathologic Physiology of Diabetes." The closing lecture of the Spring quarter was a dynamic presentation by Dr. Walter

Alvarez on "The Art of Diagnosis with the Eyes and Ears."

Several films were exhibited. Many interested students and faculty viewed: "Medicine in the Tropics," "Cardiac Arrhythmias," "Atomic Medical Cases," "Clinical Malaria," and "Cancer of the Breast." More films are planned for the future now that the vast film library of the AMA has been made available to us.

New officers and faculty advisors for the 1952-53 season were elected at a recent meeting. They are: President, Arthur Matles; Vice-President, Michael West; Treasurer, A. J. Malerstein; Secretary, Theodore Feldman. The advisors include Dr. A. H. Ryan, Dr. R. V. Milliser, and Dr. H. H. Garner. Membership now includes 140 students.

VALEDICTUM

It is with a feeling of both regret and achievement that I take leave of my office as Editor-in-Chief of the QUARTERLY. In this position for the past two years I have endeavored to improve this publication and I hope that I have attained my objective.

During my administration there have been several accessions to the journal. In terms of quantity, the size of each issue has been increased from 40 to 48 pages. I trust that the quality of the supplementary material has proved worthwhile. Clinicopathologic conferences are being published regularly; this feature is proving to be a popular section of the journal. An Abstracts section has been recently instituted for the benefit of those readers who are interested in the research being done at the School. The circulation of this publication has shown an increment of several hundred so that our present circulation totals about 2,600. We can be proud of, and take courage in these numbers, for they include readers from all parts of the world.

An editor must be concerned not only with the magnitude of his journal's followers but also with their interests. The character of the QUARTERLY'S attendance is indeed composite, consisting of students, clinicians and research workers. To satisfy these various medical factions I have attempted to obtain a fair sampling of material both clinical and academic.

The purpose of a periodical such as the QUARTERLY is twofold: not only to disperse information gathered by one or many investigators but also to stimulate productive research. Concerning the latter intent, I am primarily alluding to the younger faculty members and to the alumni of The Chicago Medical School. The QUARTERLY is an offspring of a specific institution and its maintenance depends upon those capable of proper investigation, recording and interpretation. I expect that they will continue to display increasing concern for their journal and contribute regularly to its contents.

I want to wish the new editor, Arthur Pinchuck, much success; I feel confident that his deeds and effectuations will far surpass mine.

I would like to thank my very cooperative staff, in particular, Montague Lane and Murray Rosenberg, without whom I could have accomplished nothing. Their exploits and endeavors have made the journal's success theirs — the inadequacies are mine.

At this time I am taking the opportunity to express my deep gratitude to the School Administration and to the Faculty Advisory Board of the QUARTERLY for their kind cooperation and encouraging assistance. Their guidance in all difficult matters has helped immensely to lighten an editor's burden.

Thus, I offer my farewells to the QUARTERLY and its parent institute. I hope I have contributed to the merit of both.

Maurice H. Laszlo

The following interneship appointments have been announced by the National Interassociation Committee on Interneships, Dr. F. J. Mullin, Chairman, for the Class of 1952 of The Chicago Medical School:

Arnold, Milton I.
Los Angeles County
Harbor General Hospital
Torrance, California

Behrman, Jack
Maimonides Hospital
Brooklyn 19, New York

Bernstein, Aaron
Jewish Hospital of St. Louis
St. Louis 10, Missouri

Bernstein, Martin
Jackson Memorial Hospital
Miami 36, Florida

Blass, Norman H.
Mount Sinai Hospital
Chicago, Illinois

Bragman, Robert D.
St. Frances Hospital
Evanston, Illinois

Cohen, Sanford I.
Jackson Memorial Hospital
Miami 36, Florida

Cohn, Stuart L.
Cook County Hospital
Chicago 12, Illinois

Dorin, Harold C.
Los Angeles County
Harbor General Hospital
Torrance, California

Douglas, Gilbert W.
Presbyterian Hosp. of Chicago
Chicago 12, Illinois

Ehrlich, George E.
Michael Reese Hospital
Chicago 16, Illinois

Fein, Harold
Flushing Hosp. and Dispensary
Flushing 55, New York

Fierer, Eugene H.
Jewish Hospital of Brooklyn
Brooklyn 16, New York

Finkel, Marion J.
Medical Center, Jersey City
Hospital
Jersey City 4, New Jersey

Gassel, Myron
Kings County Hospital
Brooklyn 3, New York

Golden, Emanuel L.
Jewish Hospital of Brooklyn
Brooklyn 16, New York

Goldminz, Abraham E.
Beth Israel Hospital
New York City 3, New York

Grier, Arnold
Cook County Hospital
Chicago 12, Illinois

Griesbach, Peter H.
Queens General Hospital
Jamaica 2, New York

Jagust, Joseph R.
Queens General Hospital
Jamaica 2, New York

Josel, Mark
Queens General Hospital
Jamaica 2, New York

Kaiser, Herbert S.
Queens General Hospital
Jamaica 2, New York

Kaplan, Nathan
Morristown Mem. Hospital
Morristown, New Jersey

Katz, Robert
Jewish Hospital of Brooklyn
Brooklyn 16, New York

Kessel, Elton
Cook County Hospital
Chicago 12, Illinois

Kitt, Walter
Cook County Hospital
Chicago 12, Illinois

Kowal, Roland A.
St. Mary Nazareth Hospital
Chicago 22, Illinois

Krasner, Bernard
Kings County Hospital
Brooklyn 3, New York

Krimmer, Burton M.
Michael Reese Hospital
Chicago 16, Illinois

Ladenheim, Jacob S.
Cook County Hospital
Chicago 12, Illinois

Lane, Montague
Jewish Hospital of Brooklyn
Brooklyn 3, New York

Laszlo, Maurice H.
Jewish Hospital of Brooklyn
Brooklyn 3, New York

Lee, Edmon B.
Queens General Hospital
Jamaica 2, New York

Levinson, Melvin
Jackson Memorial Hospital
Miami 36, Florida

Levy, Leslie J.
Montefiore Hospital
Pittsburgh 13, Pennsylvania

Levy, Reinhardt D.
Montefiore Hospital
Pittsburgh 13, Pennsylvania

Loeb, Sheldon
Mount Sinai Hospital
Cleveland 6, Ohio

Markowitz, Marvin
Queens General Hospital
Jamaica 2, New York

Metrick, Seymour
Mount Sinai Hospital
Chicago, Illinois

Meyer, George D.
Beth El Hospital
Brooklyn 12, New York

Mitteldorf, Julian W.
Cook County Hospital
Chicago 12, Illinois

Neustadter, Murray I.
Queens General Hospital
Jamaica 2, New York

Paul, Lloyd J.
Harper Hospital
Detroit 1, Michigan

Penner, Bernhard
Harper Hospital
Detroit 1, Michigan

Radley, Herbert S.
Harper Hospital
Detroit 1, Michigan

Rangell, Nelson
Flushing Hosp. and Dispensary
Flushing 55, New York

Ratner, Harold
Jewish Hospital of Brooklyn
Brooklyn 16, New York

Rosenberg, Irving D.
City Hospital
Newark 7, New Jersey

Rosenberg, Murray K.
Jewish Hospital of Brooklyn
Brooklyn 16, New York

Roshe, Joseph
The Mount Sinai Hospital
New York 29, New York

Rosner, Henry
Meadowbrook Hospital
Hempstead, New York

Sabramsky, Richard
Mount Sinai Hospital
Chicago, Illinois

Sathmary, Marie N.
Jewish Hospital of Brooklyn
Brooklyn 16, New York

Scheinerman, Arnold E.
Mount Sinai Hospital
Chicago, Illinois

Schrier, Robert I.
Kings County Hospital
Brooklyn 3, New York

Schuchter, Sidney L.
Philadelphia General Hospital
Philadelphia 4, Pennsylvania

Schulman, David
Kings County Hospital
Brooklyn 3, New York

Schwartz, Lester
Cook County Hospital
Chicago 12, Illinois

Stanson, Morton P.
Cedars of Lebanon Hospital
Los Angeles 29, California

Tannenbaum, Robert L.
Mount Sinai Hospital
Cleveland 6, Ohio

Tobin, Arnold D.
Harper Hospital
Detroit 1, Michigan

Wagner, Stephen
Grasslands Hospital
Valhalla, New York

Wattenmaker, Bernard
Jewish Hospital of Brooklyn
Brooklyn 16, New York

Weissman, Edward
Queens General Hospital
Jamaica 2, New York

Zinn, Alexander N.
Cook County Hospital
Chicago 12, Illinois

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